

FIG. 1

GGATCCCTGCTCCAGCAGCTGCAAGGTGCAAGAAGAAGAAGATCCCAGGGAGGAAAAATGTG	120
CTGGAGACCCTGTGTCTGGTTCCTGTGGCTTTGGTCTATCTGTCTTATGTTCAAGCAGT	180
GCCTATCCAGAAAGTCCAGGATGACACCAAAACCCCTCATCAAGACCATTGTCACCAGGAT	240
CAATGACATTTACACACGCGTATCCGCCAAGCAGAGGGTCACTGGCTTGGACTT	300
CATTCTGGGCTTCACCCCATTCTGAGTTTGTCCAAGATGGACCAGACTCTGGCAGTCTA	360
TCAACAGGTCTCACCAGCCTGCCTTCCCAAAATGTGCTGCAGATAGCCAATGACCTGGA	420
GAATCTCCGAGACCTCCTCCATCTGCTGGCCTTCTCCAAGAGCTGCTCCCTGCCTCAGAC	480
CAGTGGCCTGCAGAAGCCAGAGAGCCTGGATGGCGTCTGGAAGCCTCACTCTACTCCAC	540
AGAGGTGGTGGCTTTGAGCAGGCTGCAGGGCTCTCTGCAGGACATTCTTCAACAGTTGGA	600
TGTTAGCCCTGAATGCTGAAGTTTCAAAGGCCACCAGGCTCCCAAGAATCATGTAGAGGG	660
V S P E C *	167
AAGAAACCTTGGCTTCCAGGGGTCTTCAGGAGAAGAGAGCCATGTGCACACATCCATCAT	720
TCATTTCTCTCCCTCCTGTAGACCACCCATCCAAAGGCATGACTCCACAATGCTTGACTC	780
AAGTTATCCACACAACCTTCATGAGCACAAGGAGGGGCCAGCCTGCAGAGGGGACTCTCAC	840
CTAGTTCTTCAGCAAGTAGAGATAAGAGCCATCCCATCCCTCCATGTCCACCTGCTCC	900
GGGTACATGTTCTCCGTGGGTACACGCTTCGCTGCGGCCAGGAGAGGTGAGGTAGGGA	960
TGGGTAGAGCCTTTGGGCTGTCTCAGAGTCTTTGGGAGCACCGTGAAGGCTGCATCCACA	1020
CACAGCTGGAAACTCCCAAGCAGCACACGATGGAAGCACTTATTTATTTATTCTGCATTC	1080
TATTTTGGATGGATCTGAAGCAAGGCATCAGCTTTTTCAGGCTTTGGGGGTGAGCCAGGA	1140
TGAGGAAGGCTCCTGGGGTGCTGCTTTCAATCCTATTGATGGGTCTGCCCAGGCAAACC	1200
TAATTTTGGAGTACTGGAAGGAAGGTGGGATCTTCCAAACAAGAGTCTATGCAGGTAG	1260
CGCTCAAGATTGACCTCTGGTGACTGGTTTTGTTTCTATTGTGACTGACTCTATCCAAAC	1320
ACGTTTGCAGCGGCATTGCCGGGAGCATAGGCTAGGTTATTATCAAAAGCAGATGAATTT	1380
TGTCAGAGTGAATATGTATCTATGTGCACCTGAGGGTAGAGGATGTGTTAGAGGGAGGGT	1440
GAAGGATCCGGAAGTGTCTCTGAATTACATATGTGTGGTAGGCTTTTCTGAAAGGGTGA	1500
GGCATTTTCTTACCTCTGTGGCCACATAGTGTGGCTTTGTGAAAAGGACAAAGGAGTTGA	1560
CTCTTTCCGGAACATTTGGAGTGTACCAGGCACCCCTGGAGGGGCTAAAGCTACAGGCCT	1620
TTTGTGGCATATTGCTGAGCTCAGGGAGTGAGGGCCCCACATTTGAGACAGTGAGCCCC	1680
AAGAAAAGGGTCCCTGGTGTAGATCTCCAAGGTTGTCCAGGGTTGATCTCACAATGCGTT	1740
TCCTAAGCAGGTAGACGTTTGCATGCCAATATGTGGTTCTCATCTGATTGGTTTCATCAA	1800
AGTAGAACCCTGCTCCTCCACCCATTCTGTGGGGAGTTTTGTTCAGTGGAATGAGAAAT	1860
CACTTAGCAGATGGTCCCTGAGCCCTGGGCCAGCACTGCTGAGGAAGTGCCAGGGCCCCAG	1920
GCCAGGCTGCCAGAAATGCCCTTCGGGCTGGAGGATGAACAAAGGGGCTTGGGTTTTTCC	1980
ATCACCCCTGCACCCATATGTCACCATCAAACCTGGGGGGCAGATCAGTGAGAGGACATTG	2040
ATGGAAAGCAATACACTTTAAGACTGAGCAGAGTTTCGTGCTCAGCTCTGTCTGGTGCTG	2100
TGAGCTAGAGAAGCTCACCACATACATATAAAAATCAGAGGCTCATGTCCCTGTGGTTAG	2160
ACCTTACTCGCGCGGTGTACTCCACCACAGCAGCACCGCACCGCTGGAAGTACAGTGCT	2220
GTCCTTCAACAGGTGTGAAAGAACCCTGAGCTGAGGGTGACAGTGCCCAGGGGAACCCTGCT	2280
TGCAGTCTATTGCATTTACATACCGCATTTTCAGGGCACATTAGCATCCACTCCTATGGTA	2340
GCACACTGTTGACAATAGGACAAGGGATAGGGGTTGACTATCCCTTATCCAAAATGCTTG	2400
GGACTAGAAGAGTTTTGGATTTTAGAGTCTTTTCAGGCATAGGTATATTTGAGTATATAT	2460
AAAATGAGATATCTTGGGGATGGGGCCCCAAGTATAAACATGAAGTTCATTTATATTTTCAT	2520
AATACCGTATAGACACTGCTTGAAGTGTAGTTTTTATACAGTGTTTTAAATAACGTTGTAT	2580
GCATGAAAGACGTTTTTACAGCATGAACCTGTCTACTCATGCCAGCACTCAAAAACCTTG	2640
GGGTTTTGGAGCAGTTTGGATCTTGGGTTTTCTGTTAAGAGATGGTTAGCTTATACCTAA	2700
AACCATAATGGCAAACAGGCTGCAGGACCAGACTGGATCCTCAGCCCTGAAGTGTGCCCT	2760
TCCAGCCAGGTCATACCCTGTGGAGGTGAGCGGGATCAGGTTTTGTGGTGCTAAGAGAGG	2820
AGTTGGAGGTAGATTTTGGAGGATCTGAGGGC	2852

---G--GTTG	CAAGGCCCAA	GAAGCCCA--	-TCCTGGGAA	GGAAAATGCA	50
TTGGGGAACC	CTGTG-CGGA	TTCTTGTGGC	TTTGGCCCTA	TCTTTTCTAT	100
GTCCAAGCTG	TGCCCATCCA	AAAAGTCCAA	GATGACACCA	AAACCCTCAT	150
CAAGACAATT	GTCACCAGGA	TCAATGACAT	TTCACACACG	CAGTCAGTCT	200
CCTCCAAACA	GAAAGTCACC	GGTTTGGACT	TCATTCTCTG	GCTCCACCCC	250
ATCCTGACCT	TATCCAAGAT	GGACCAGACA	CTGGCAGTCT	ACCAACAGAT	300
CCTCACCAGT	ATGCCTTCCA	GAAACGTGAT	CCAAATATCC	AACGACCTGG	350
AGAACCTCCG	GGATCTTCTT	CACGTGCTGG	CCTTCTCTAA	GAGCTGCCAC	400
TTGCCCTGGG	CCAGTGGCCT	GGAGACCTTG	GACAGCCTGG	GGGGTGTCTT	450
GGAAGCTTCA	GGCTACTCCA	CAGAGGTGGT	GGCCCTGAGC	AGGCTGCAGG	500
GGTCTCTGCA	GGACATGCTG	TGGCAGCTGG	ACCTCAGCCC	TGGGTGCTGA	550
GGCCTTGAAG	GTCACTCTTC	CTGCAAGGAC	T-ACGTTAAG	GGAAGGAACT	600
CTGGTTTCCA	GGTATCTCCA	GGATTGAAGA	GCATTGCATG	GACACCCCTT	650
ATCCAGGACT	CTGTCAATTT	CCCTGACTCC	TCTAAGCCAC	TCTTCCAAAG	700
G					701

FIG. 2

1 MET HIS TRP GLY THR LEU CYS GLY PHE LEU TRP LEU TRP PRO TYR
16 LEU PHE TYR VAL GLN ALA VAL PRO ILE GLN LYS VAL GLN ASP ASP
31 THR LYS THR LEU ILE LYS THR ILE VAL THR ARG ILE ASN ASP ILE
46 SER HIS THR GLN SER VAL SER SER LYS GLN LYS VAL THR GLY LEU
61 ASP PHE ILE PRO GLY LEU HIS PRO ILE LEU THR LEU SER LYS MET
76 ASP GLN THR LEU ALA VAL TYR GLN GLN ILE LEU THR SER MET PRO
91 SER ARG ASN VAL ILE GLN ILE SER ASN ASP LEU GLU ASN LEU ARG
106 ASP LEU LEU HIS VAL LEU ALA PHE SER LYS SER CYS HIS LEU PRO
121 TRP ALA SER GLY LEU GLU THR LEU ASP SER LEU GLY GLY VAL LEU
136 GLU ALA SER GLY TYR SER THR GLU VAL VAL ALA LEU SER ARG LEU
151 GLN GLY SER LEU GLN ASP MET LEU TRP GLN LEU ASP LEU SER PRO
166 GLY CYS END

FIG. 3

MOUSE	MCWRPLCRFL	WLWSYLSYVQ	AVPIQKVODD	TKTLIKTIYT	RINDISHTQS	50
	☆ ☆ ☆	☆ ☆				
HUMAN	MHWGTLGGFL	WLWPYLFYVQ	AVPIQKVODD	TKTLIKTIYT	RINDISHTQS	
MOUSE	VSAKORVTGL	DFIPGLHPIL	SLSKMDOTLA	VYQQVLTSLP	SONVLOIAND	100
	☆		-	-	☆ ☆	
HUMAN	VSSKQKVTGL	DFIPGLHPIL	TLSKMDOTLA	VYQQILTSMF	SRNVIOISND	
MOUSE	LENLRDLLHL	LAFSKSCSLP	QTSGLOKPE\$	LDGVLEASLY	STEVVALSRL	150
		☆	** ☆☆☆	☆		
HUMAN	LENLRDLLHV	LAFSKSCHLP	WASGLETLDS	LGGVLEASGY	STEVVALSRL	
MOUSE	QGSLODILQQ	LDVSPEC				167
	- ☆	- ☆				
HUMAN	QGSLODMLWQ	LDLSPGC				

FIG.4

1 MET CYS TRP ARG PRO LEU CYS ARG PHE LEU TRP LEU TRP SER TYR
16 LEU SER TYR VAL GLN ALA VAL PRO ILE GLN LYS VAL GLN ASP ASP
31 THR LYS THR LEU ILE LYS THR ILE VAL THR ARG ILE ASN ASP ILE
46 SER HIS THR SER VAL SER ALA LYS LYS GLN ARG VAL THR GLY LEU ASP
61 PHE ILE PRO GLY LEU HIS PRO ILE LEU SER LEU SER LYS MET ASP
76 GLN THR LEU ALA VAL TYR GLN GLN VAL LEU THR SER LEU PRO SER
91 GLN ASN VAL LEU GLN ILE ALA ASN ASP LEU GLU ASN LEU ARG ASP
106 LEU LEU HIS LEU LEU ALA PHE SER LYS SER CYS SER LEU PRO GLN
121 THR SER GLY LEU GLN LYS PRO GLU SER LEU ASP GLY VAL LEU GLU
136 ALA SER LEU TYR SER THR GLU VAL VAL ALA LEU SER ARG LEU GLN
151 GLY SER LEU GLN ASP ILE LEU GLN GLN LEU ASP VAL SER PRO GLU
166 CYS END

FIG.5

1 MET HIS TRP GLY THR LEU CYS GLY PHE LEU TRP LEU TRP PRO TYR
16 LEU PHE TYR VAL GLN ALA VAL PRO ILE GLN LYS VAL GLN ASP ASP
31 THR LYS THR LEU ILE LYS THR ILE VAL THR ARG ILE ASN ASP ILE
46 SER HIS THR SER VAL SER SER LYS GLN LYS VAL THR GLY LEU ASP
61 PHE ILE PRO GLY LEU HIS PRO ILE LEU THR LEU SER LYS MET ASP
76 GLN THR LEU ALA VAL TYR GLN GLN ILE LEU THR SER MET PRO SER
91 ARG ASN VAL ILE GLN ILE SER ASN ASP LEU GLU ASN LEU ARG ASP
106 LEU LEU HIS VAL LEU ALA PHE SER LYS SER CYS HIS LEU PRO TRP
121 ALA SER GLY LEU GLU THR LEU ASP SER LEU GLY GLY VAL LEU GLU
136 ALA SER GLY TYR SER THR GLU VAL VAL ALA LEU SER ARG LEU GLN
151 GLY SER LEU GLN ASP MET LEU TRP GLN LEU ASP LEU SER PRO GLY
166 CYS END

FIG.6

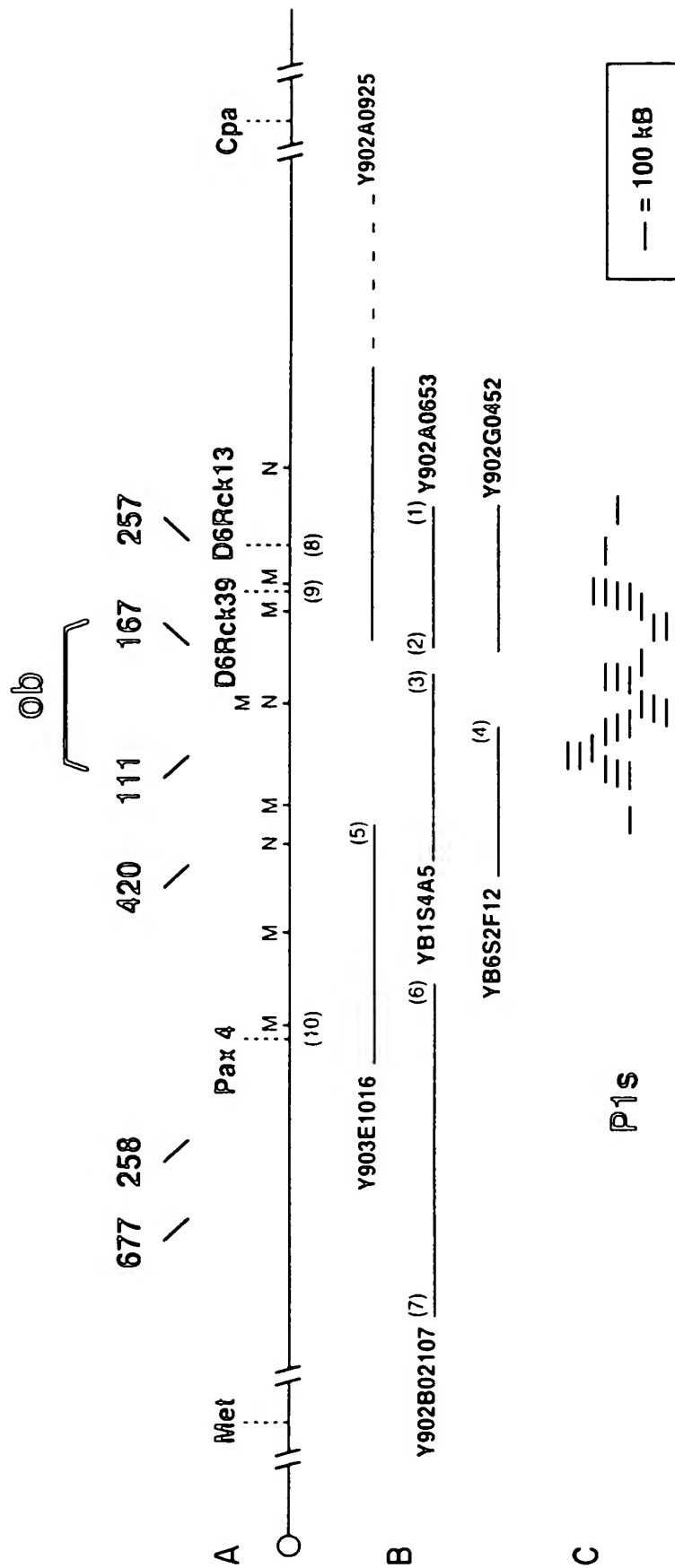


FIG. 7

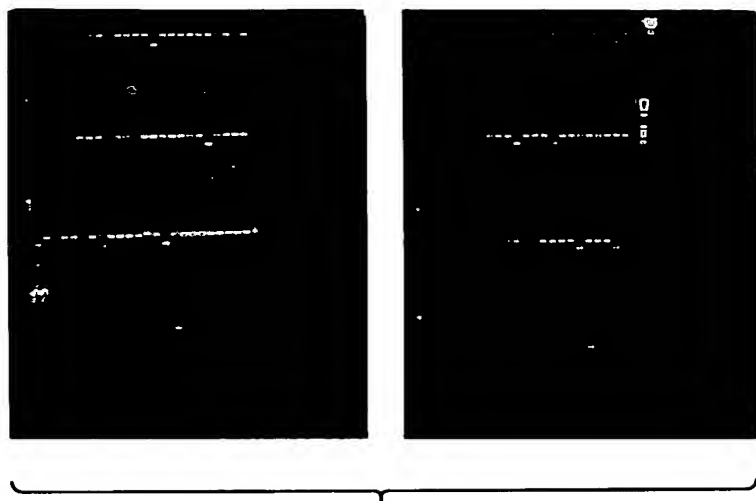


FIG.8

1 2 3 4 5 6 7

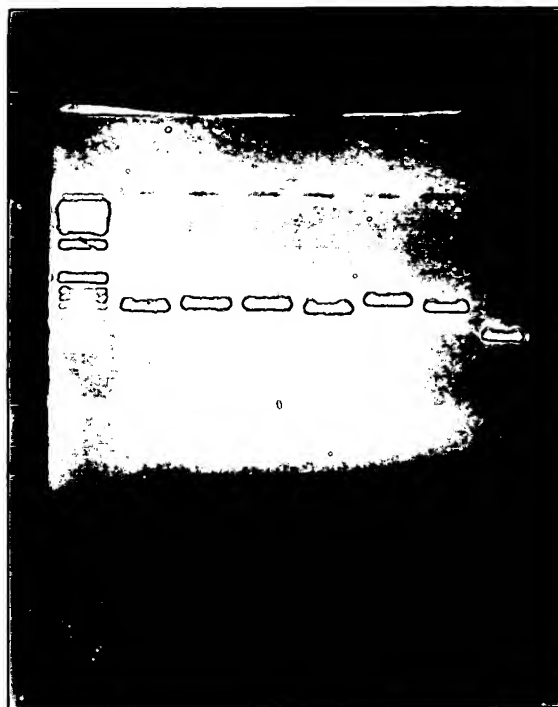


FIG.9

	+10	+20	+30	+40
1	GTGCAAGAAG	AAGAAGATCC	<u>CAGGGCAGGA</u>	<u>AAATGTGCTG</u> GAGACCCCTG
	-----	-----	-----	-----
	CACGTTCCTC	TTCTTCTAGG	GTCCCGTCTT	TTTACACGAC CTCTGGGGAC
	+10	+20	+30	+40
51	TGTCGGGTCC	NGTGGNTTTG	GTCCATCTG	TCTTATGTNC AAGCAGTGCC
	-----	-----	-----	-----
	ACAGCCCGAG	NCACCNAAAC	CAGGATAGAC	AGAATACANG TTCGTCA <u>CGG</u>
	+10	+20	+30	+40
101	TATCCAGAAA	GTCCAGGATG	ACACCAAAG	CCTCATCAAG ACCATTGTCA
	-----	-----	-----	-----
	<u>ATAGGTCCTT</u>	<u>CAGGTCCTAC</u>	TGTGGTTTTC	GGAGTAGTTC TGGTAACAGT
	+10	+20	+30	+40
151	NCAGGATCAC	TGANATTTCA	CACACG	
	-----	-----	-----	
	NGTCCTAGTG	ACTNTAAAGT	GTGTGC	

FIG.10

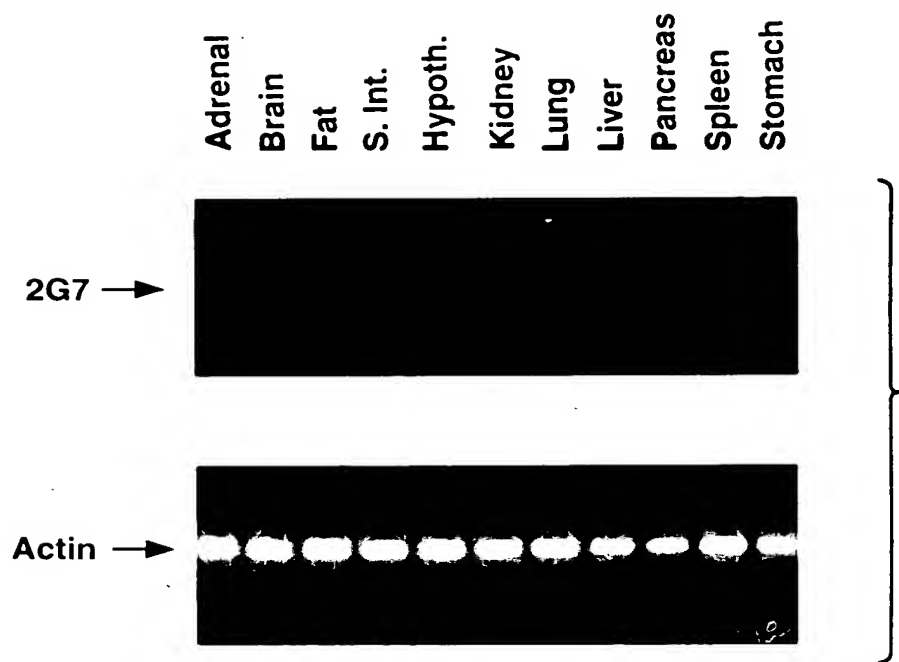


FIG. 11A

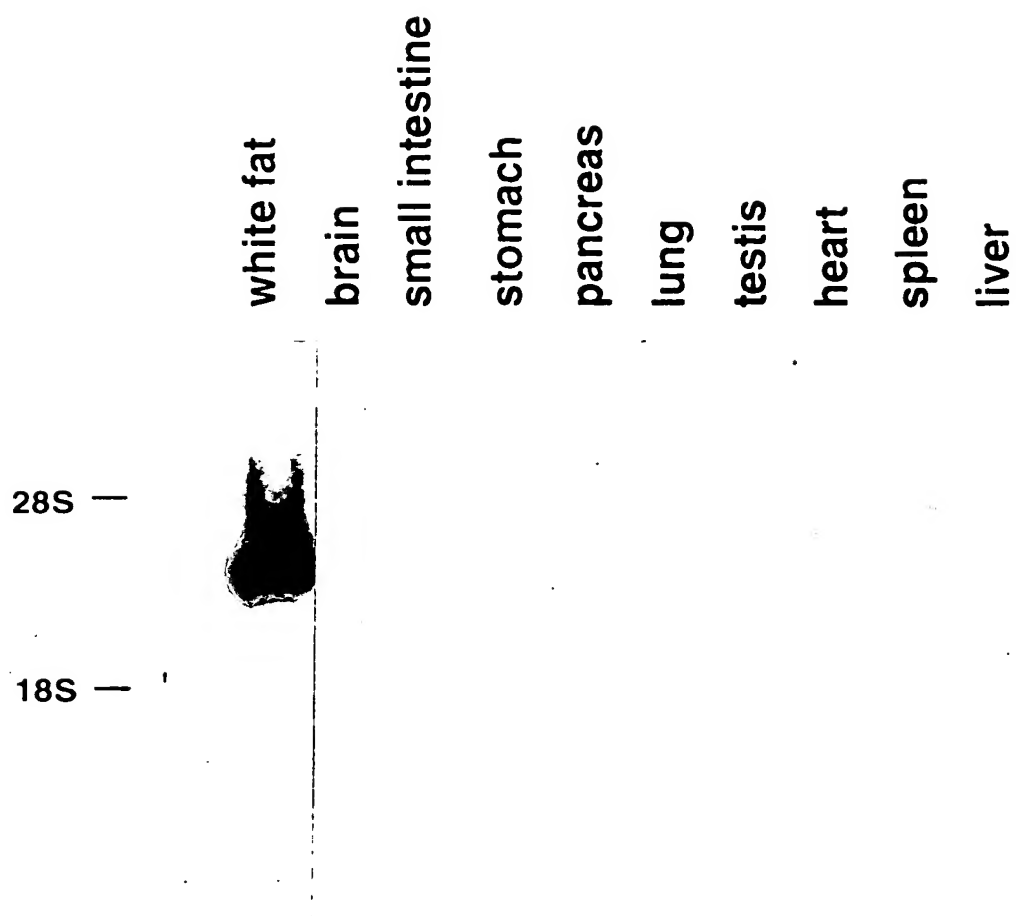


FIG.11B

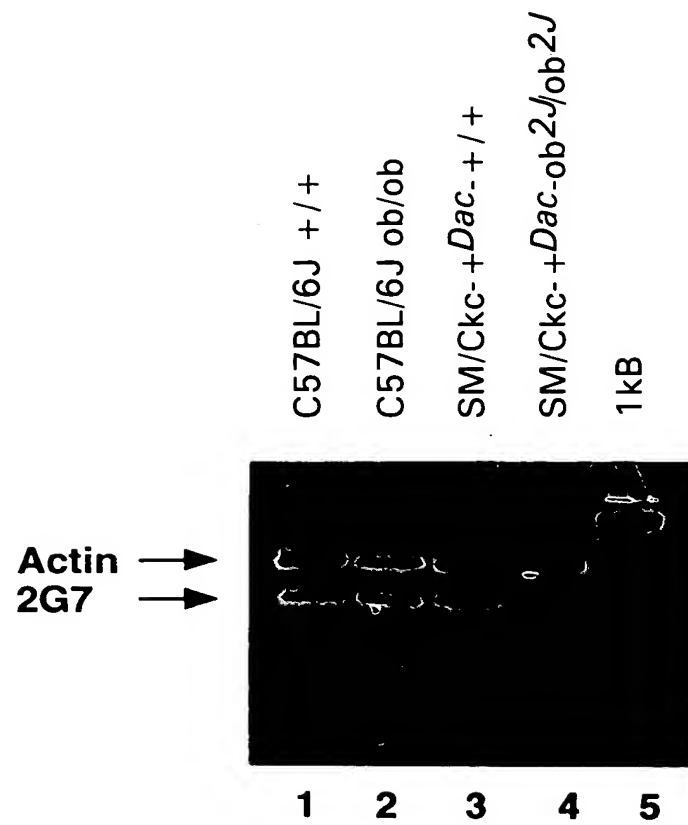


FIG.12A

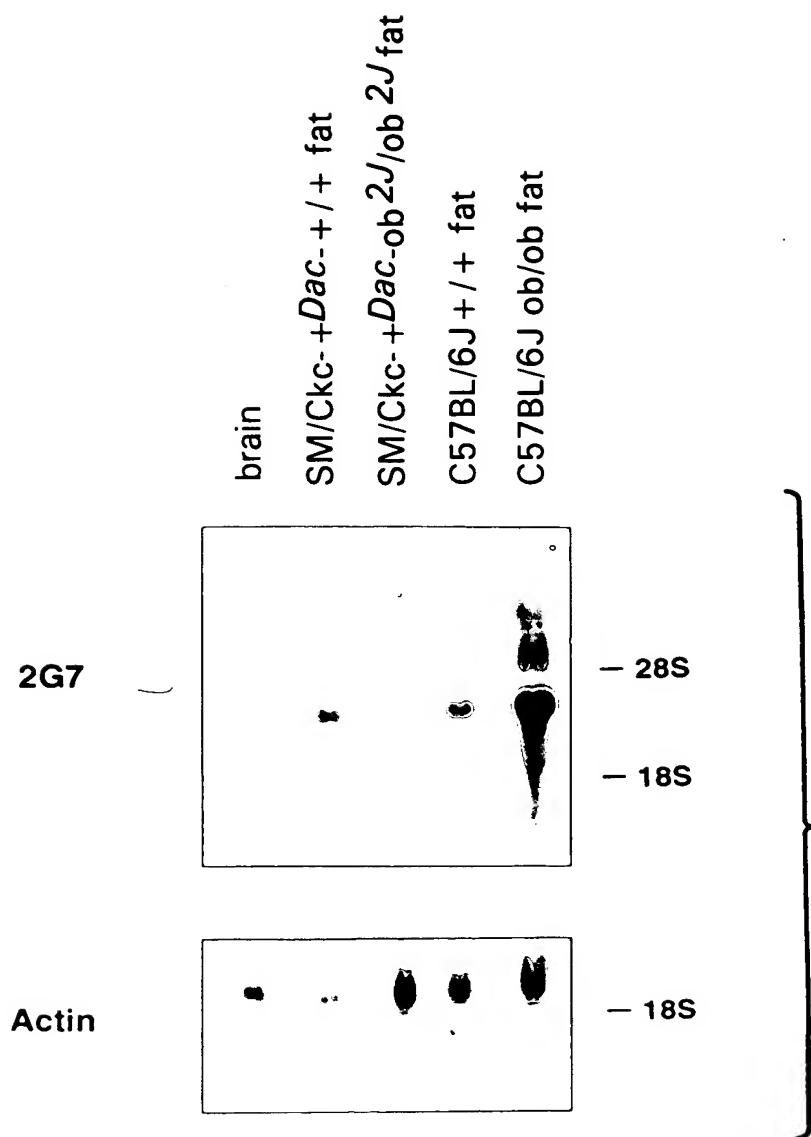


FIG.12B

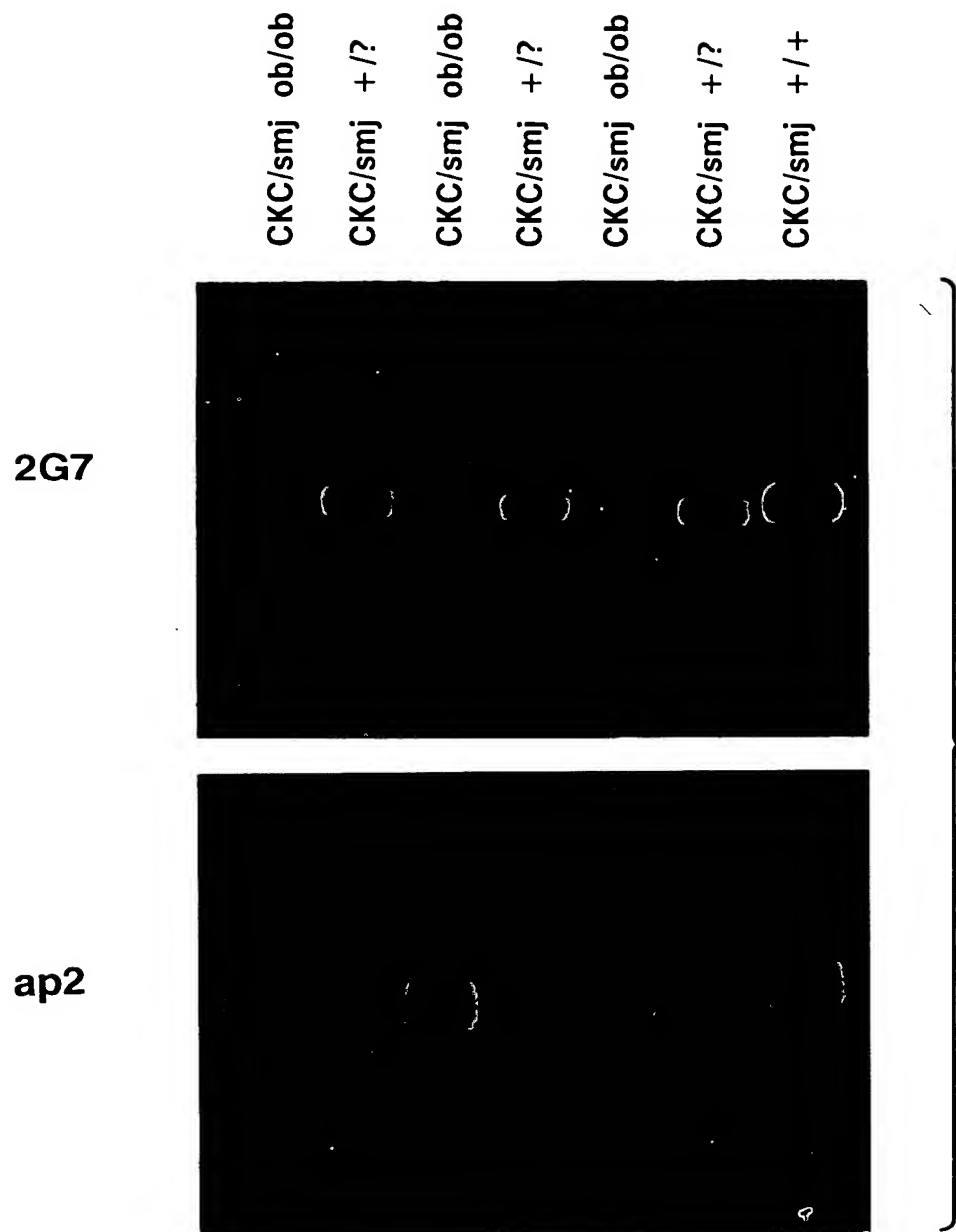


FIG. 13

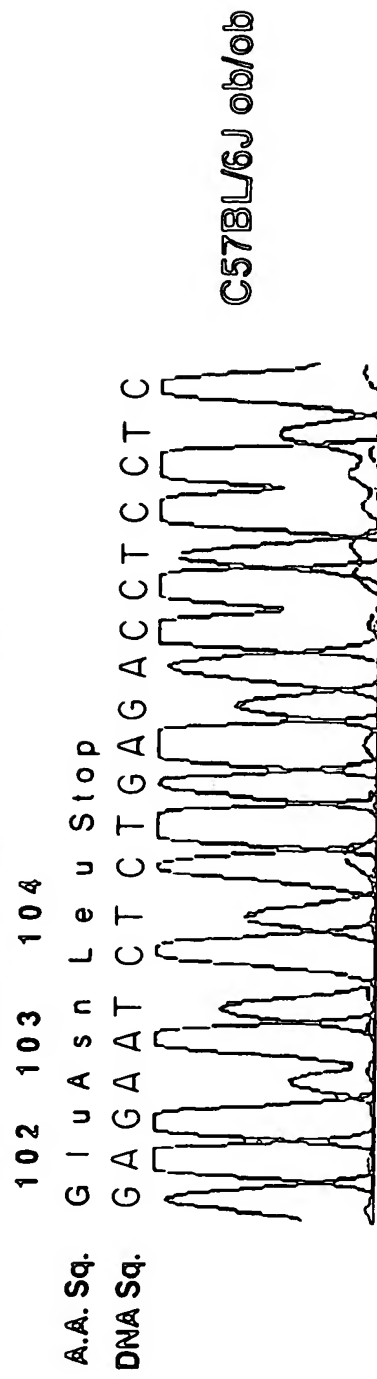
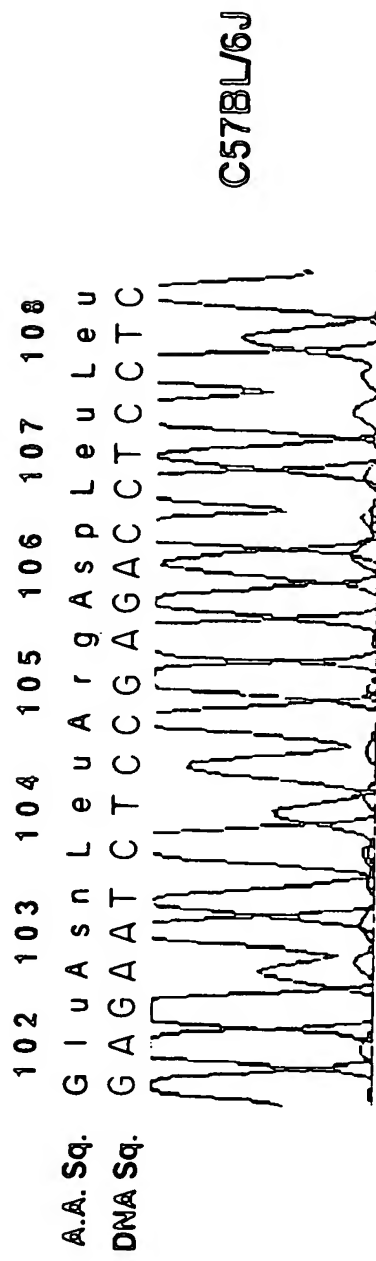


FIG.14

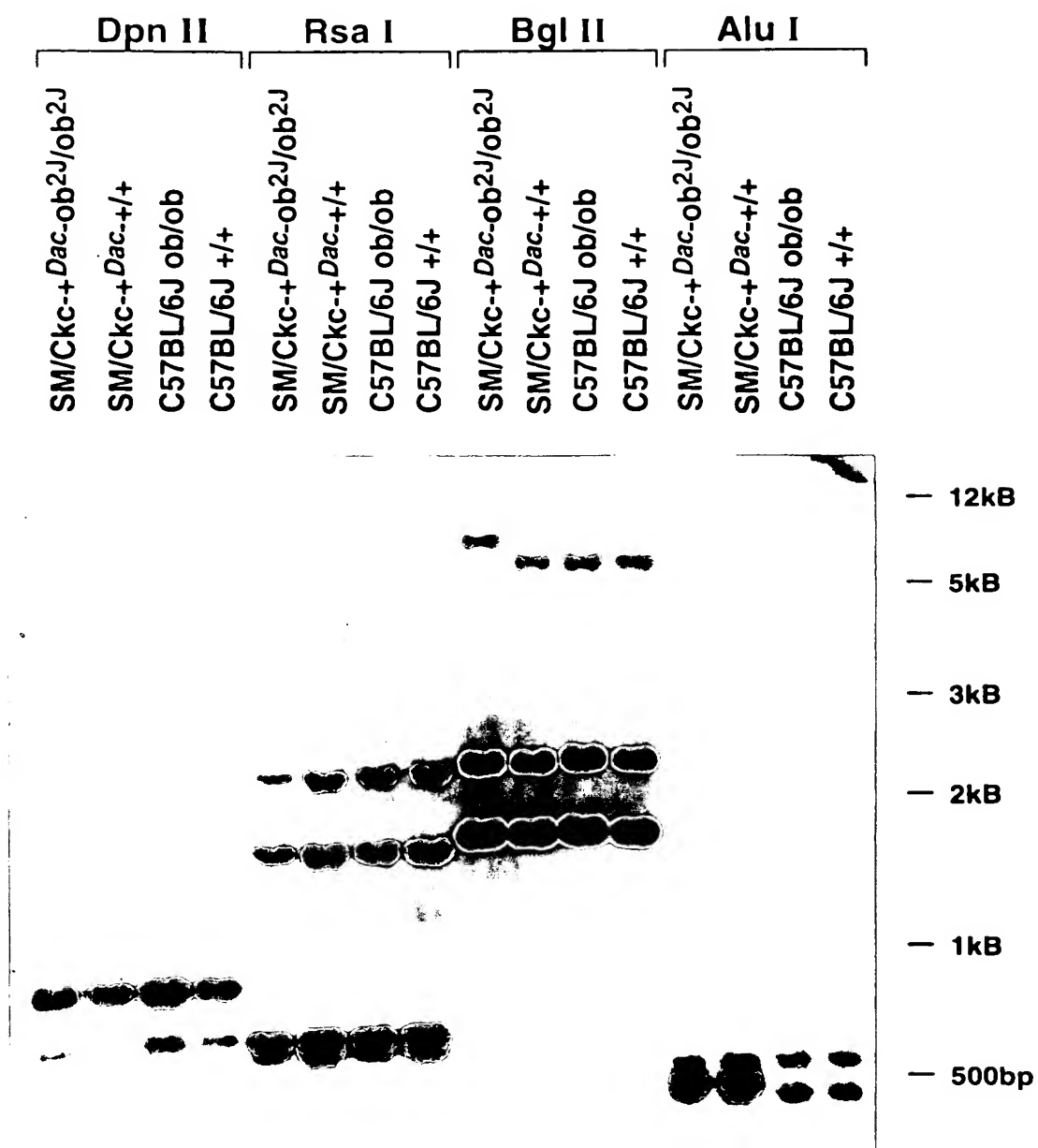


FIG.15A

BglII Digests

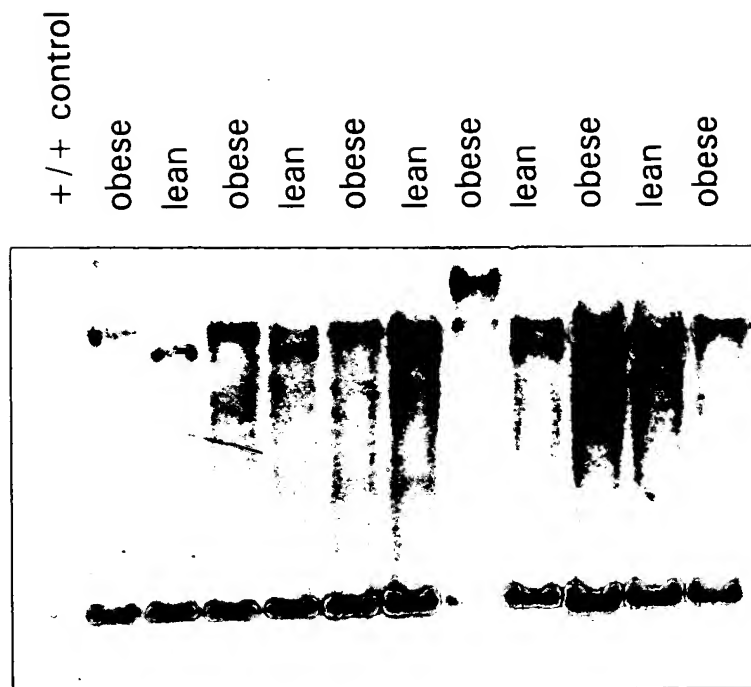


FIG.15B



FIG.16

T7 PROMOTER PRIMER 69348-1

----->

T7 PROMOTER

BGLII
AGATCTCGATCCGGCAATTAAATACGACTCACTATAGGGAATTGTGAGGGGATAACAAATCCCTCTACA

-----> LAC OPERATOR XBAI

RBS NCOI HIS-TAG
AATAATTTTGTTTAACTTTAAGAGGAGATATACCATGGGAGCAGCCATCATCATCATCACAGCAGGGC
METGLYSERSERHISHISHISHISHISSERSERGLY

NDEI XHOI BAMHI
CTGGTCCGGCGGCGCAGCCATATGCTCGAGGATCCGGCTGCTAACAAAGCCGAAAGGAGCTGAGTTGGCT
LEUVALPROARGGLYSERHISMETLEUGLUASPPROALALAASNLYSALAARGLYSGLUALAGLULEUALA
THROMBIN

Bpui1021 T7 TERMINATOR
GCTGCCACCGCTGAGCAATAACTAGCATACCCCTGGGGCCTCTAAACGGTCTTGAGGGGTTTTC
ALAAALATHRALAGLUGLNEND

<-----

T7 TERMINATOR PRIMER #69337-1

FIG.17

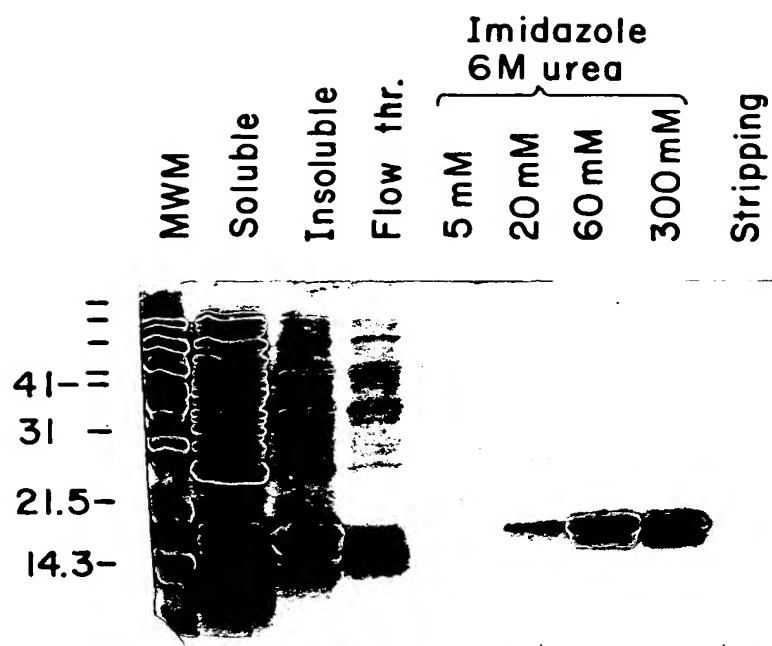


FIG.18A

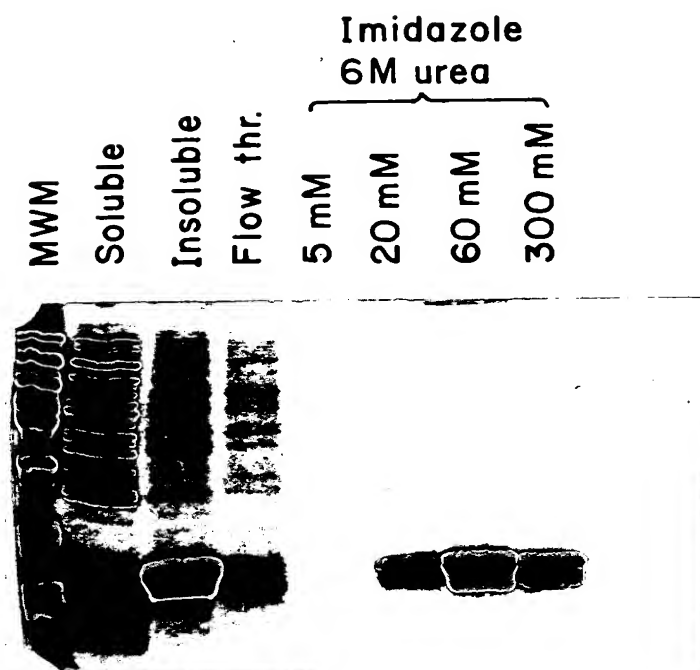


FIG.18B

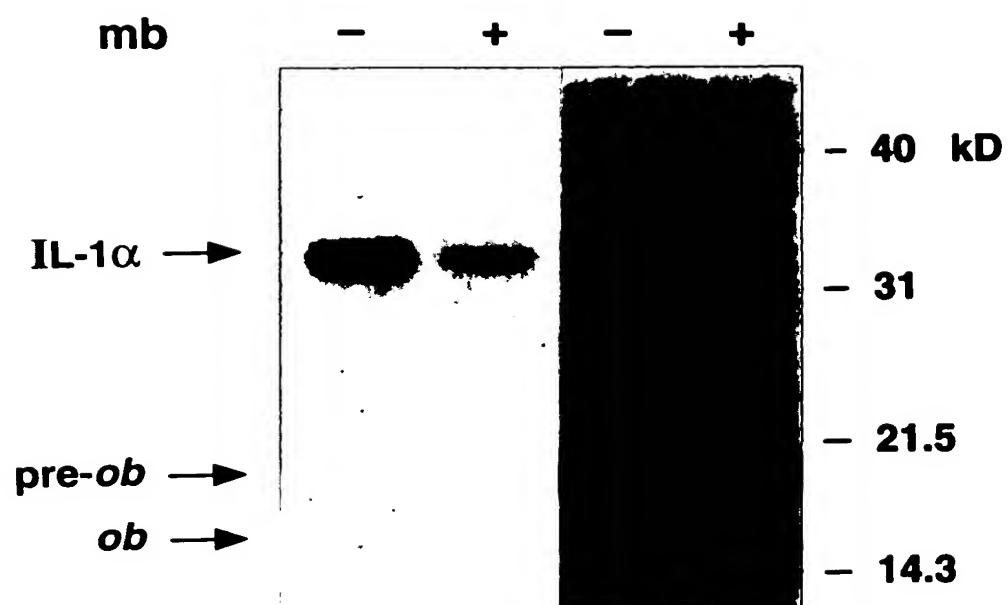


FIG.19A

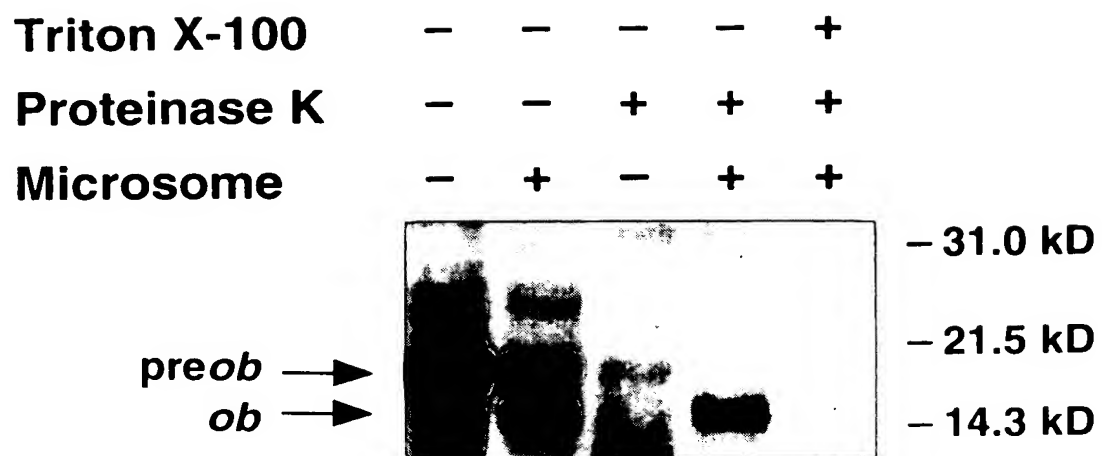


FIG.19B

10 20 30 40 50
GGTTGCAAGG CCAAGAAGC CCATCCTGGG AAGGAAATG CATTGGGGAA
 HOB 1G F → START
 60 70 80 90 100
CCCTGTGCGG ATTCTTGTGG CTTTGGCCCT ATCTTTTCTA TGTCCAAGCT
 110 120 130 140 150
GTGCCCATCC AAAAAGTCCA AGATGACACC AAAACCCCTCA TCAAGACAAT
 160 170 180 190 200
TGTCACCAGG ATCAATGACA TTTCACACAC GGTAAGGAGA GTATCGGGGG
 210 220 230 240 250
ACAAAGTAGA ACTGCAGCCA GCCCAGCACT GGCTCCTAGT GGCACTGGAC
 ← HOB 1G R

5' OF 1ST INTRON
 ↳

FIG.20A-1

260	270	280	290	300
<u>CCAGATAGTC CAAGAAACAT TTATTGAAGC CCTCCTGAAT GCCAGGCACC</u>				
310	320	330	340	350
<u>TACTGGAAGC TGAGAAGGAT TTGGATAGC ACAGGGCTCC ACTCTTTCTG</u>				
360	370	380	390	400
<u>GTTGTTTCTT NTGGCCCCCT CTGCCCTGCTG AGATNCCAGG GGTTAGNGGT</u>				
410	420	430	440	450
<u>TCCTAATTCC TAAA-----</u>				
GAP OF SEQUENCE (~1.4 KB)				
460	470	480	490	500
<u>GGTTCCTTCA GGAAGAGGCC ATGTAAGAGA AAGGAATTGA CCTAGGGAAA</u>				

FIG.20A - 2

510	520	530	540	550
<u>ATTGGCCTGG GAAGTGGAGG GAACGGATGG TGTGGGAAA GCAGGAATCT</u>				
560	570	580	590	600
<u>CGGAGACCAG CTTAGAGGCT TGGCAGTCAC CTGGTGCAG GANACAAGGG</u>				
610	620	630	640	650
<u>CCTGAGCCAA AGTGGTGAGG GAGGGTGGA GGAGACAGCC CAGAGAATGA</u>				
660	670	680	690	700
<u>CCCTCCATGC CCACGGGGAA GGCAGAGGGC TCTGAGAGCG ATTCTTCCCA</u>				
		3' OF 1ST INTRON ←		
710	720	730	740	750
<u>CATGCTGAGC ACTTGTTCTC CCTCTTCTC CTNCATAGCA GTCAGTCTCC</u>				
HOB 2G F →				

FIG.20A -3

760	770	780	790	800
<u>TCCAAACAGA AAGTCACCGG TTTGGACTTC ATTCTGGGC TCCACCCCAT</u>				
810	820	830	840	850
<u>CCTGACCTTA TCCAAGATGG ACCAGACACT GGCAGTCTAC CAACAGATCC</u>				
860	870	880	890	900
<u>TCACCAGTAT GCCTTCCAGA AACGTGATCC AAATATCCAA CGACCTGGAG</u>				
910	920	930	940	950
<u>AACCTCCGGG ATCTTCTTCA CGTGCTGGCC TTCTCTAAGA GCTGCCACTT</u>				
960	970	980	990	1000
<u>GCCCTGGGCC AGTGGCCTGG AGACCTTGGA CAGCCTGGGG GGTGTCCTGG</u>				

FIG.20A -4

1010	1020	1030	1040	1050
<u>AAGCTTCAGG C TACTCCACA GAGGTGGTGG CCCTGAGCAG GCTGCAGGGG</u>				
1060	1070	1080	1090	1100
<u>TCTCTGCAGG ACATGCTGTG GCAGCTGGAC CTCAGCCCTG GGTGCTGAGG</u>				
				<u>STOP</u>
1110	1120	1130	1140	1150
<u>CCTTGAAGGT CACTCTTCCT GCAAGGACTA CGTTAAGGA AGGAAGCTCTG</u>				
1160	1170	1180	1190	1200
<u>GCTTCCAGGT ATCTCCAGGA TTGAAGAGCA TTGCATGGAC ACCCCTTATC</u>				
	HOB 2G R			
1210	1220	1230	1240	1250
<u>CAGGACTCTG TCAATTTCCT TGACTCCTCT AAGCCACTCT TCCAAGG</u>				

FIG.20A -5

MOUSE OB STRUCTURE

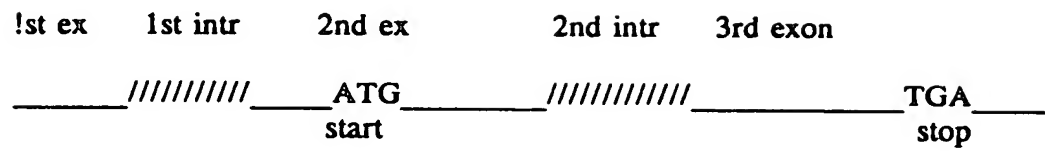


FIG.20B

HUMAN OB STRUCTURE

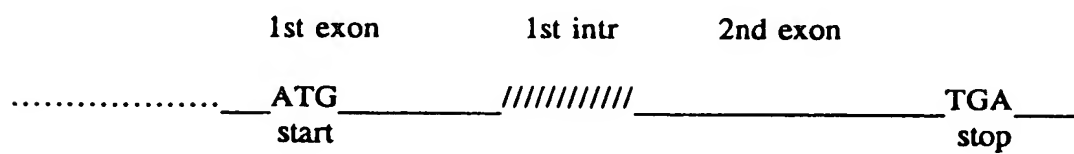


FIG.20C

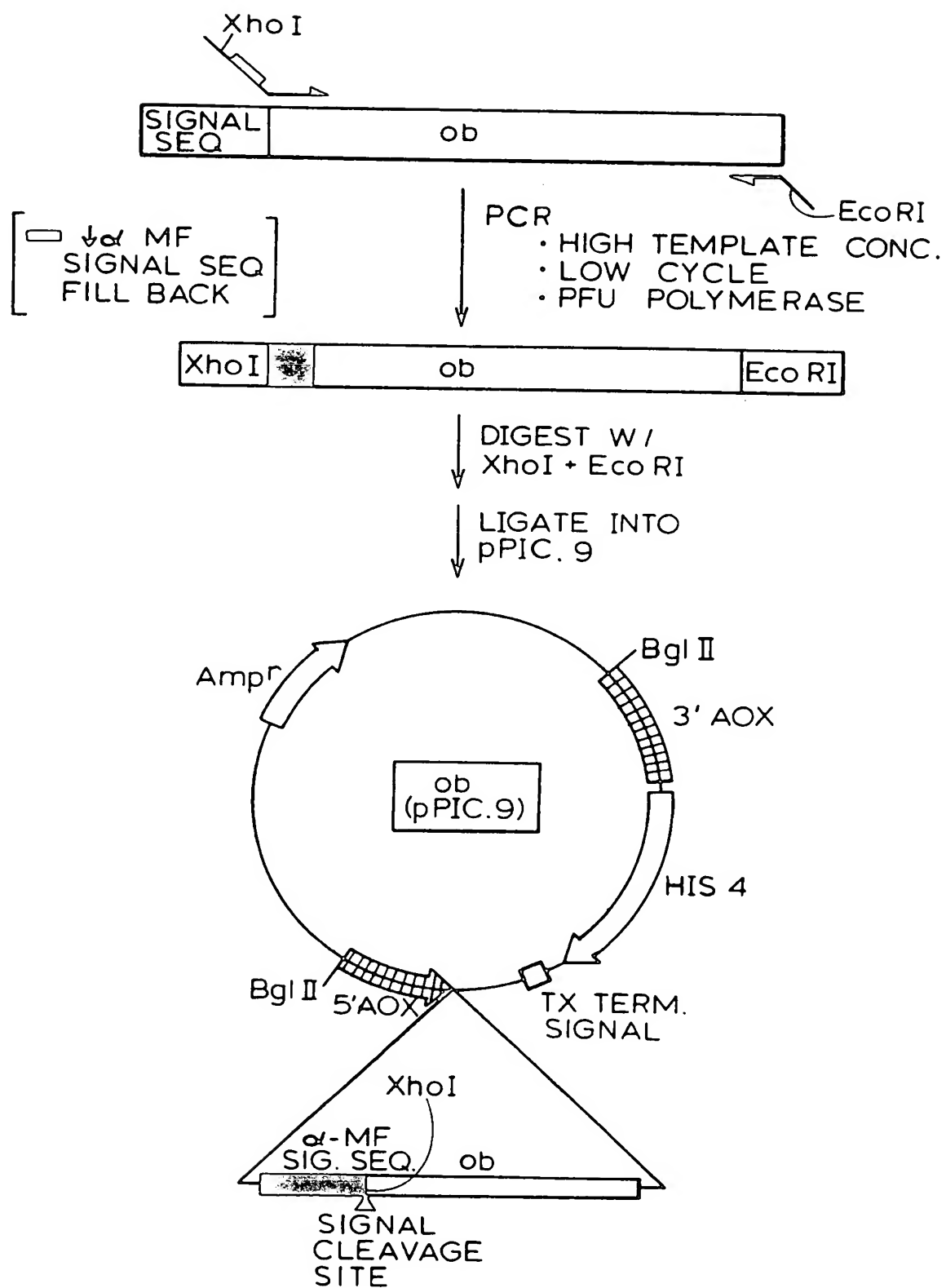


FIG.21A

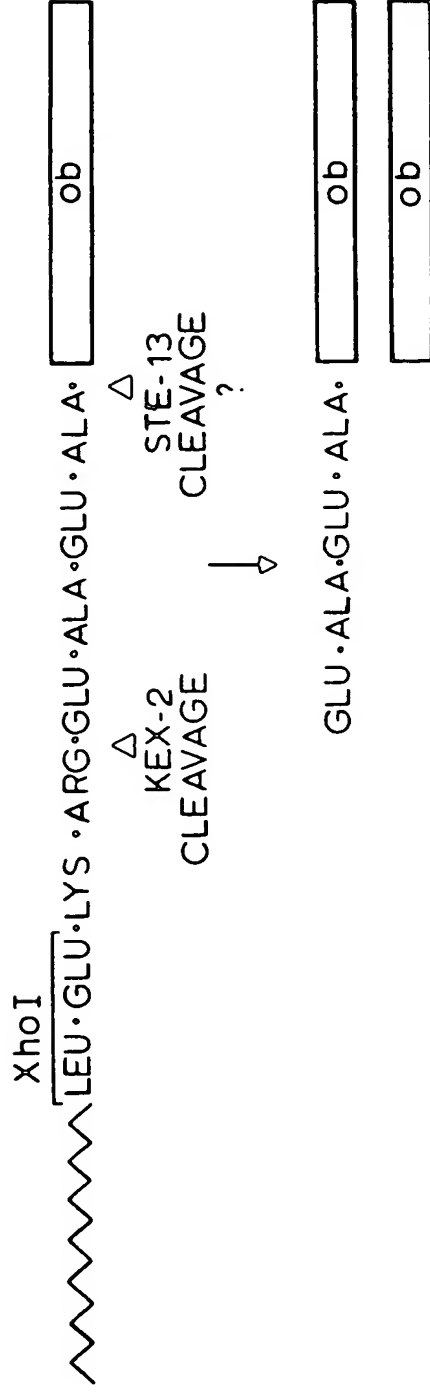


FIG. 21B

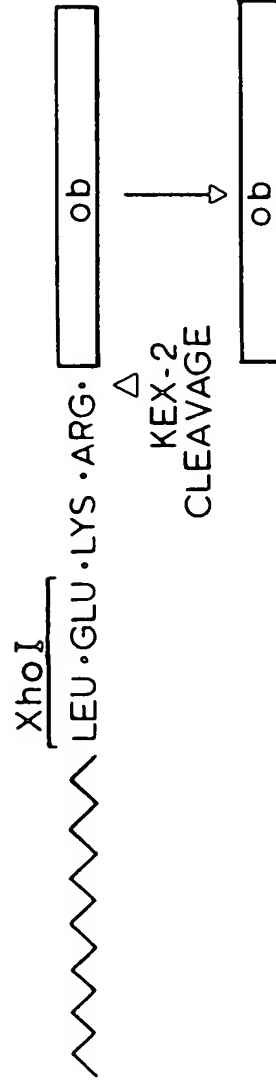


FIG. 21C

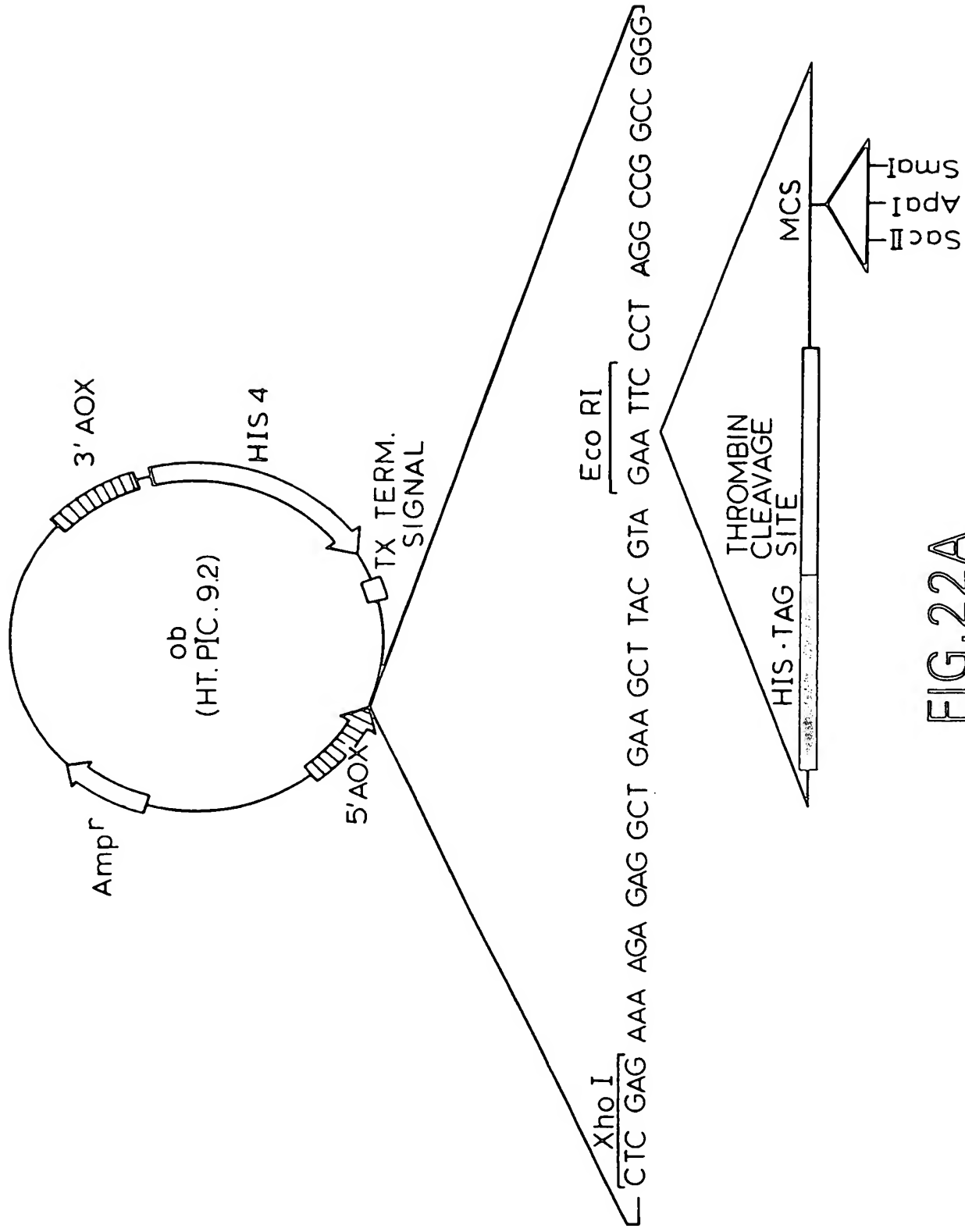


FIG. 22A

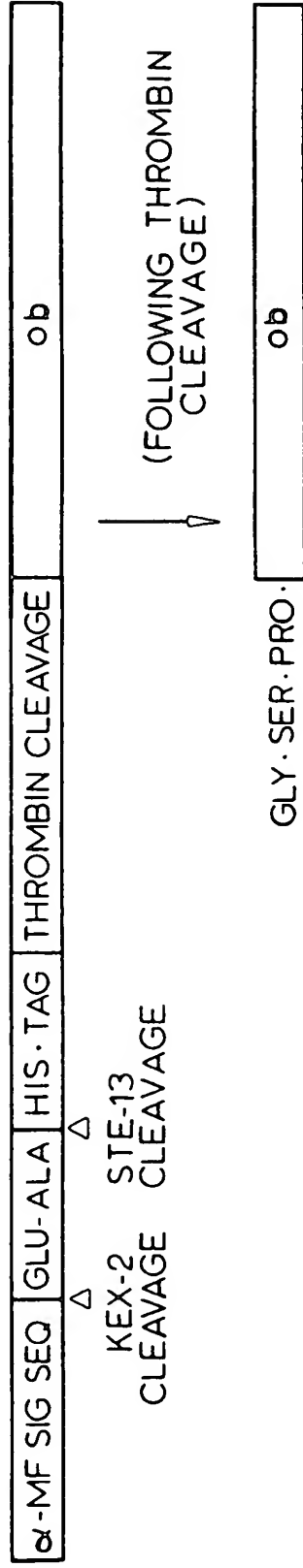


FIG. 22B

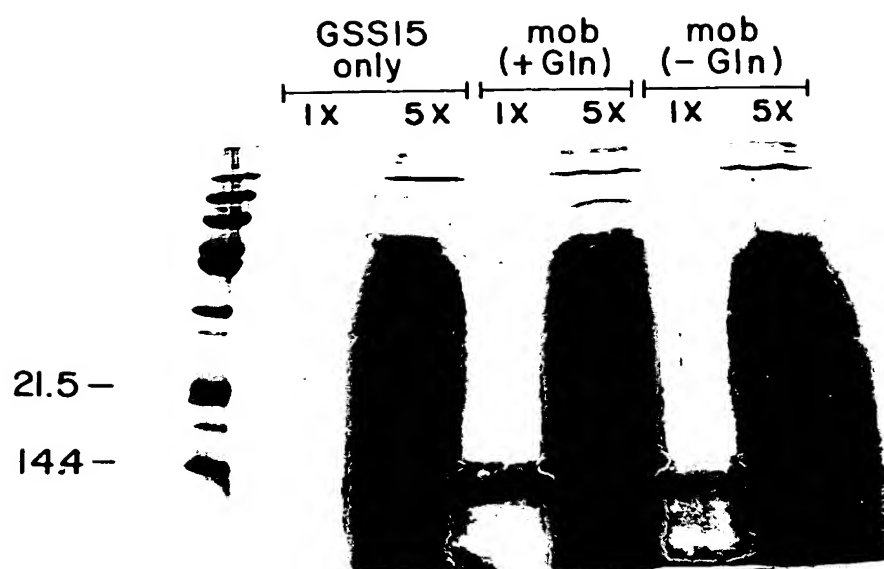


FIG.23A

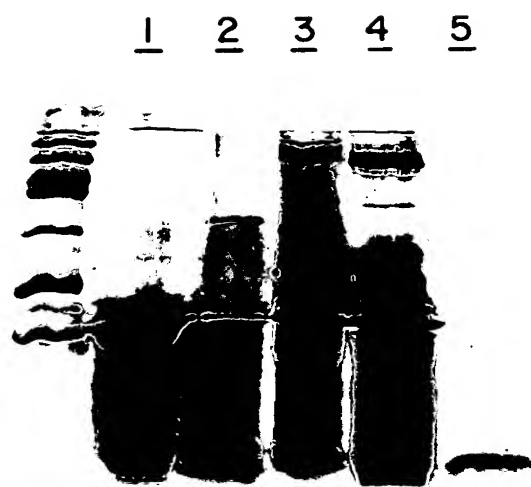


FIG.23B

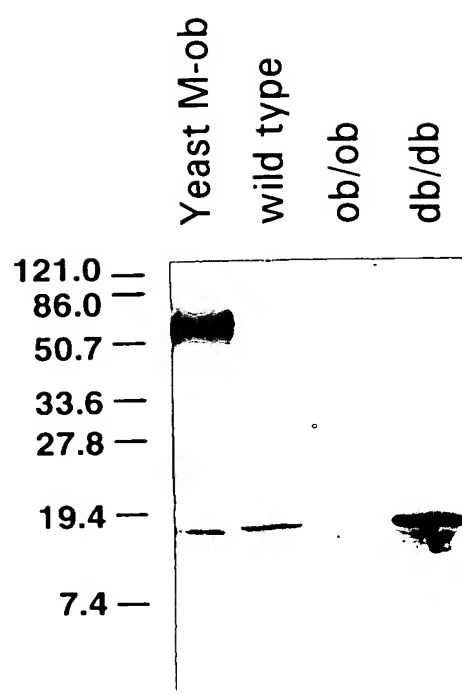


FIG.24A

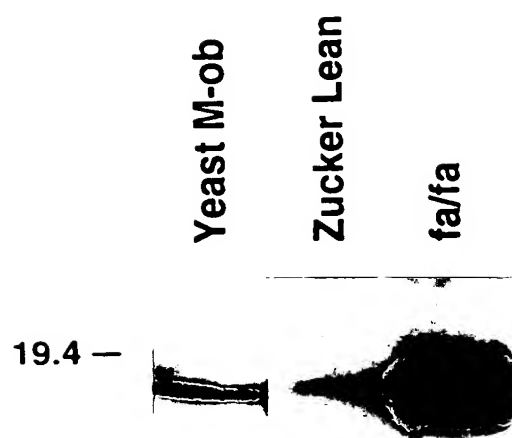


FIG.24B

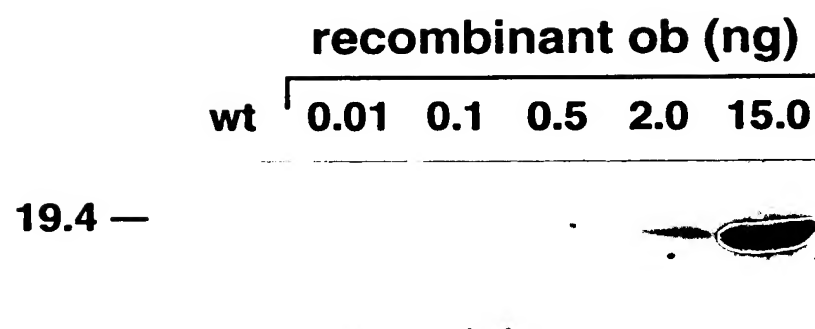


FIG.24C

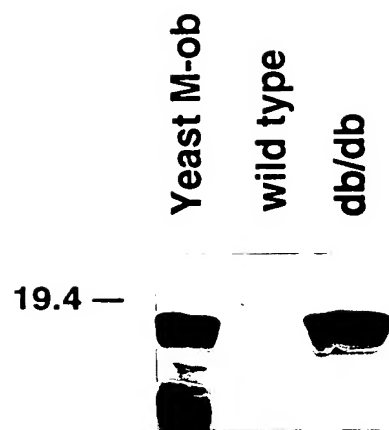


FIG.24D

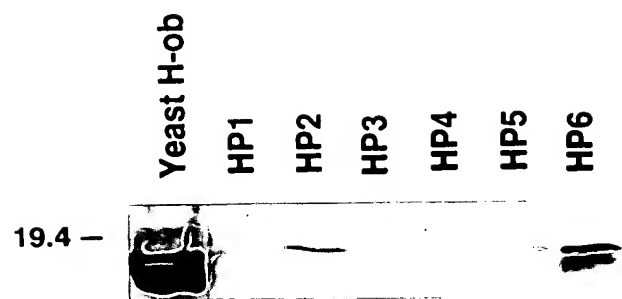


FIG.25A

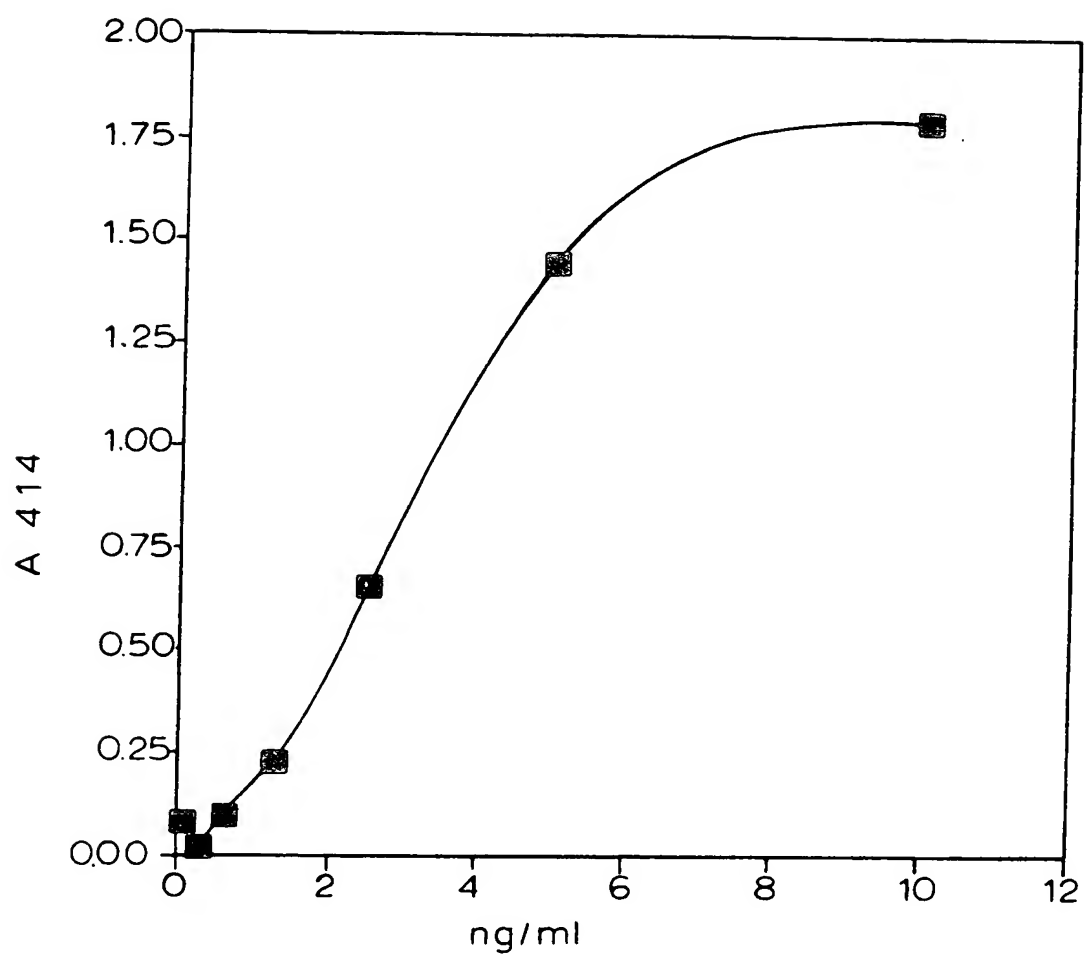


FIG.25B

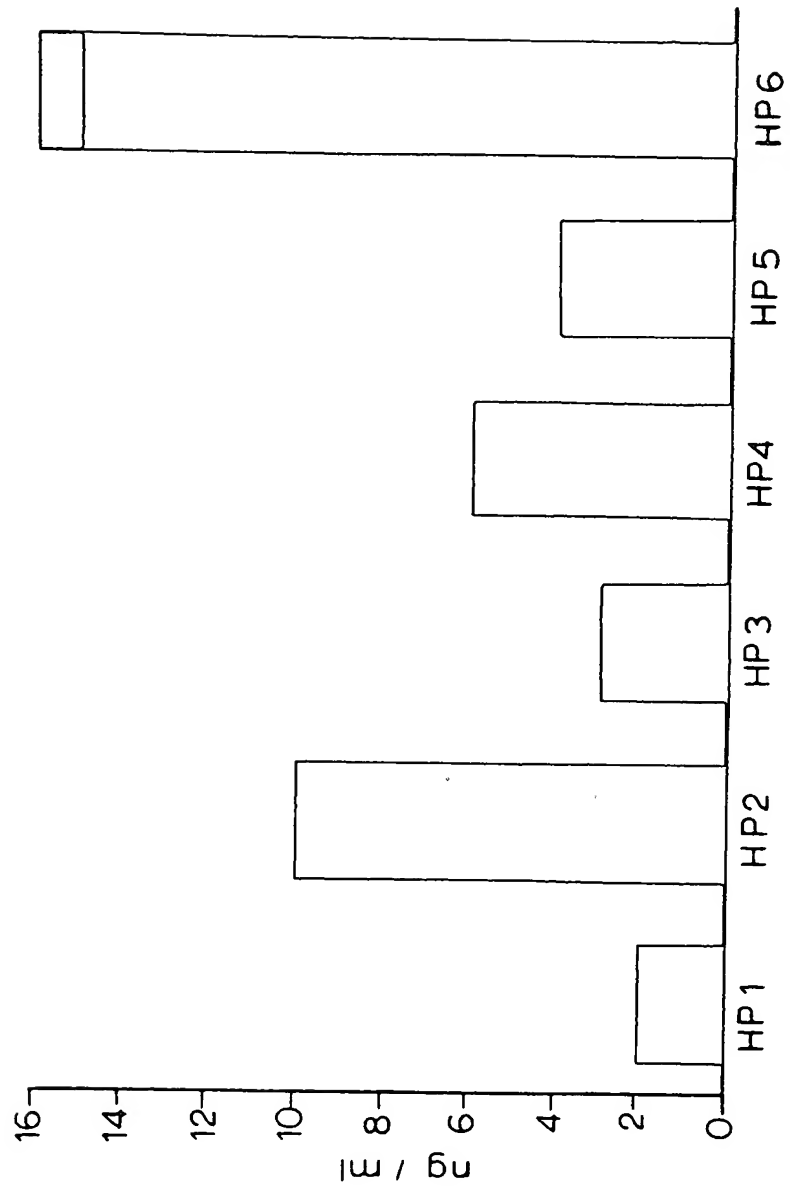


FIG.25C

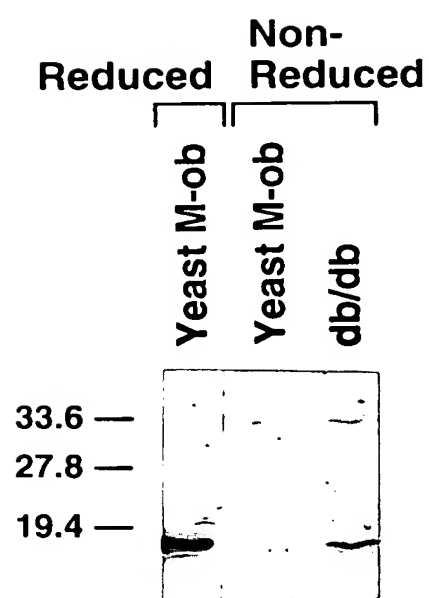
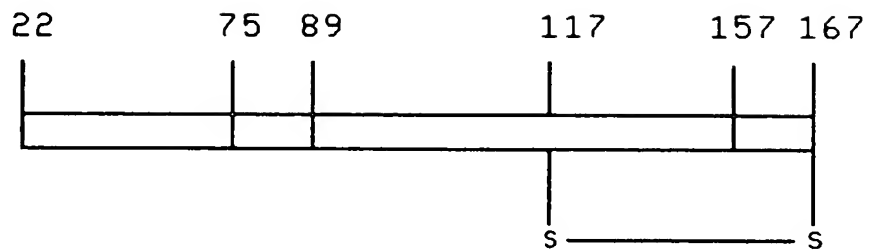


FIG.26A

Human ob



<u>Peptide</u>	<u>Mass(Da)</u>	
	Expected	Observed
22-167	16,024	$16,024 \pm 3$
22-75	5936.9	5936.6 ± 1
76-89	1562.7	N.D.
90-167	8434.5	8435.6 ± 1
158-167	1131.9	N.D.

FIG.26 B

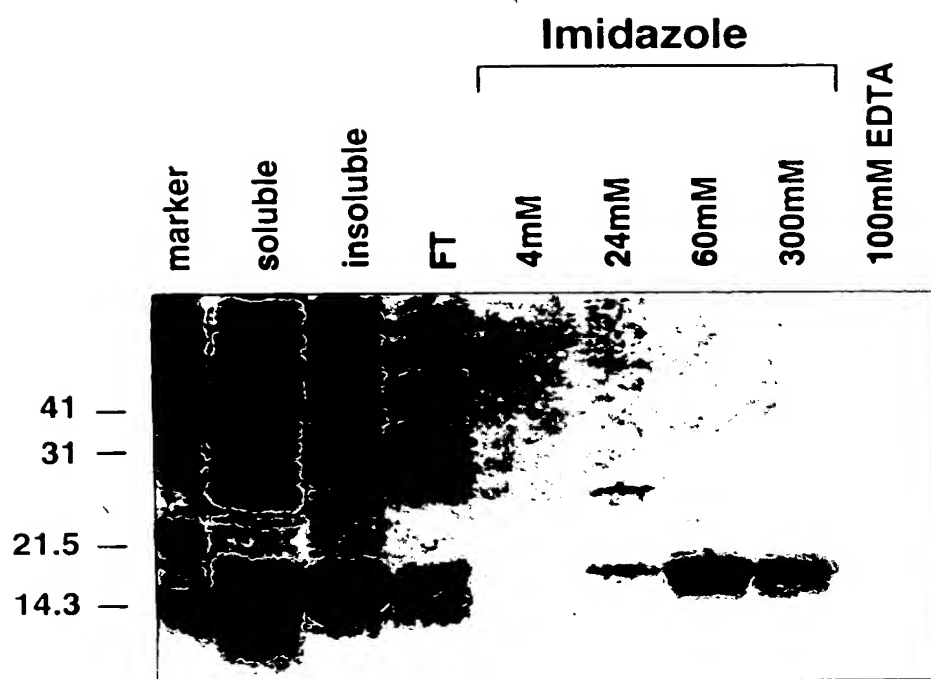


FIG.27

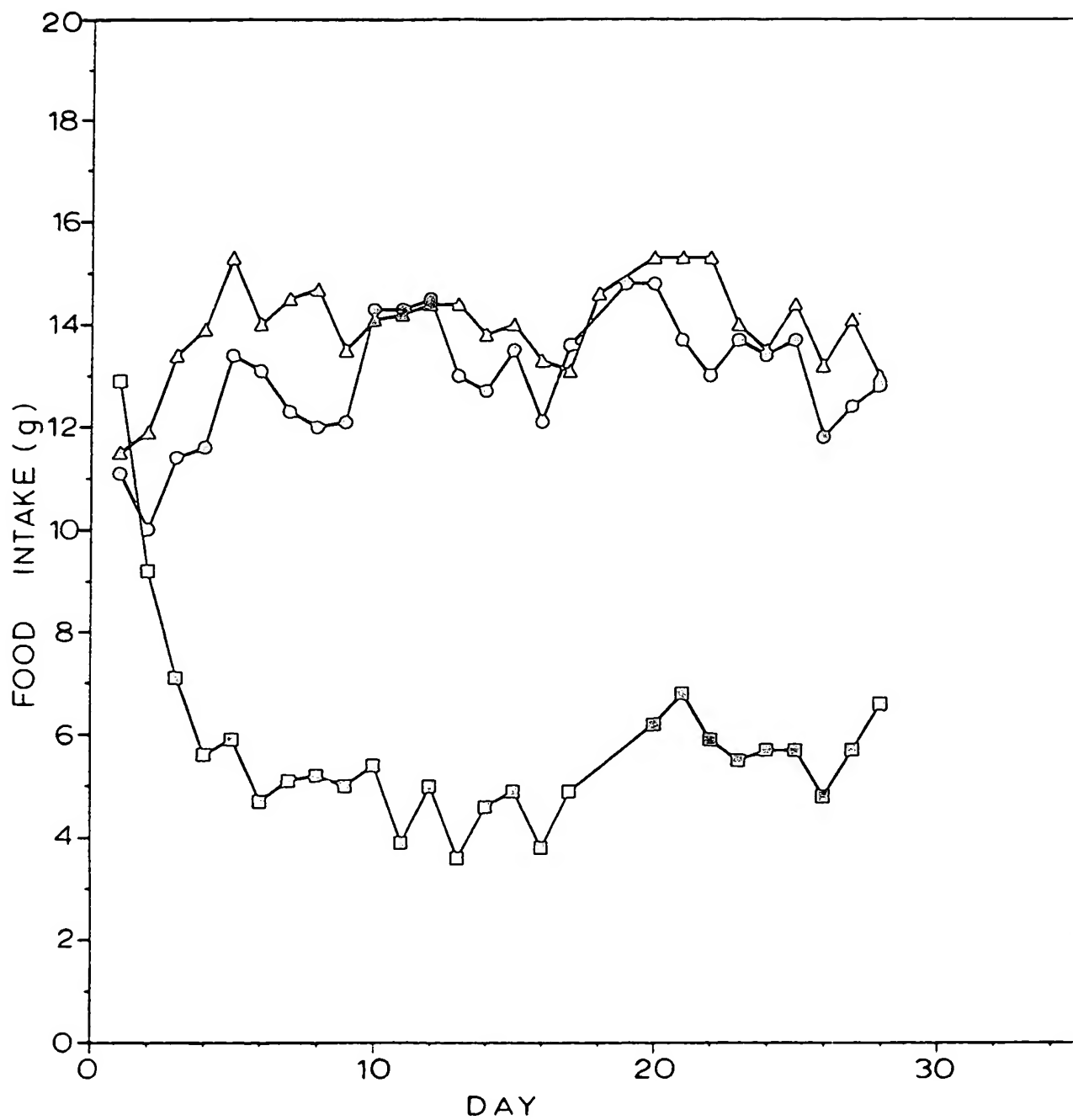


FIG.28A

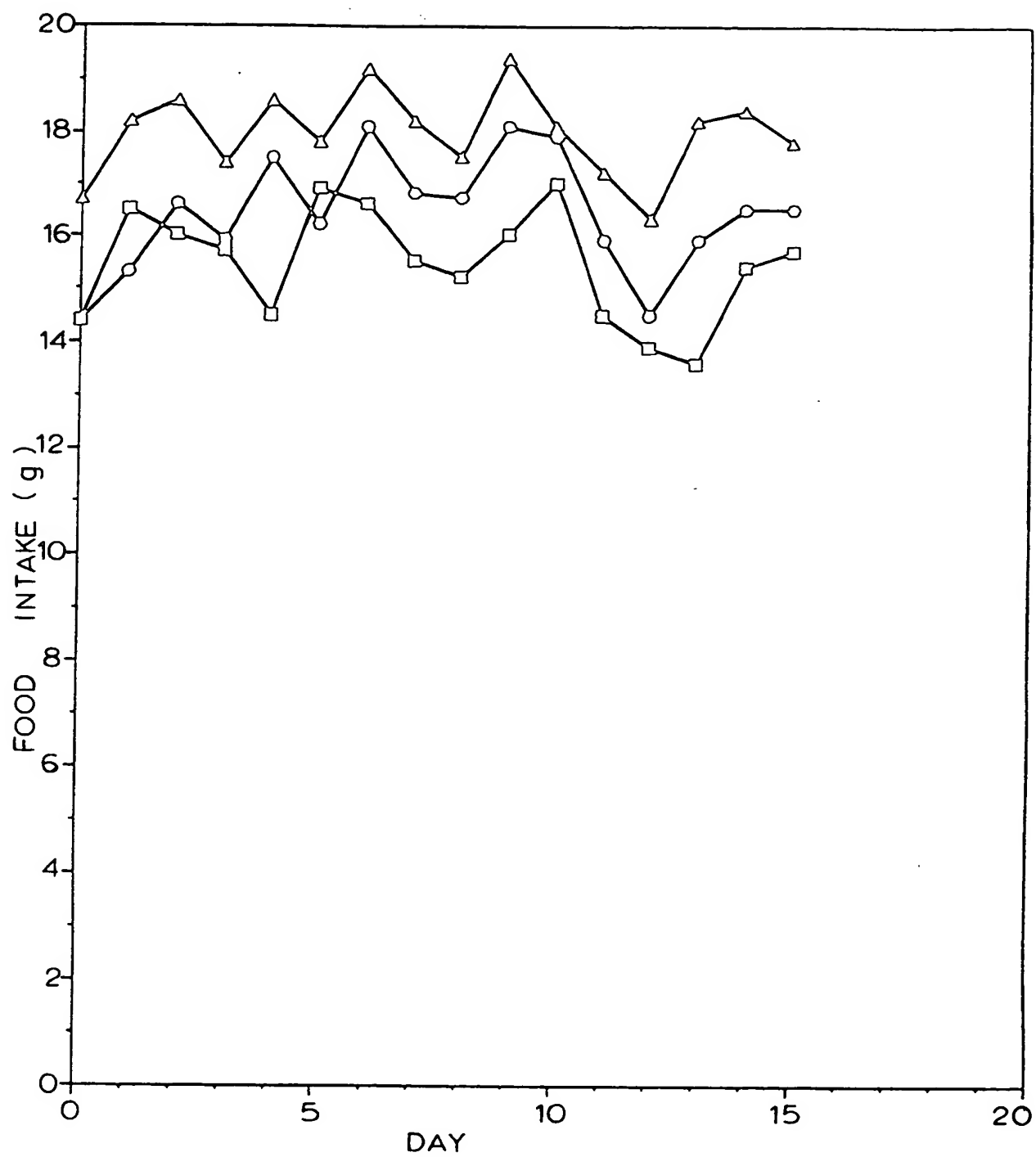


FIG.28B

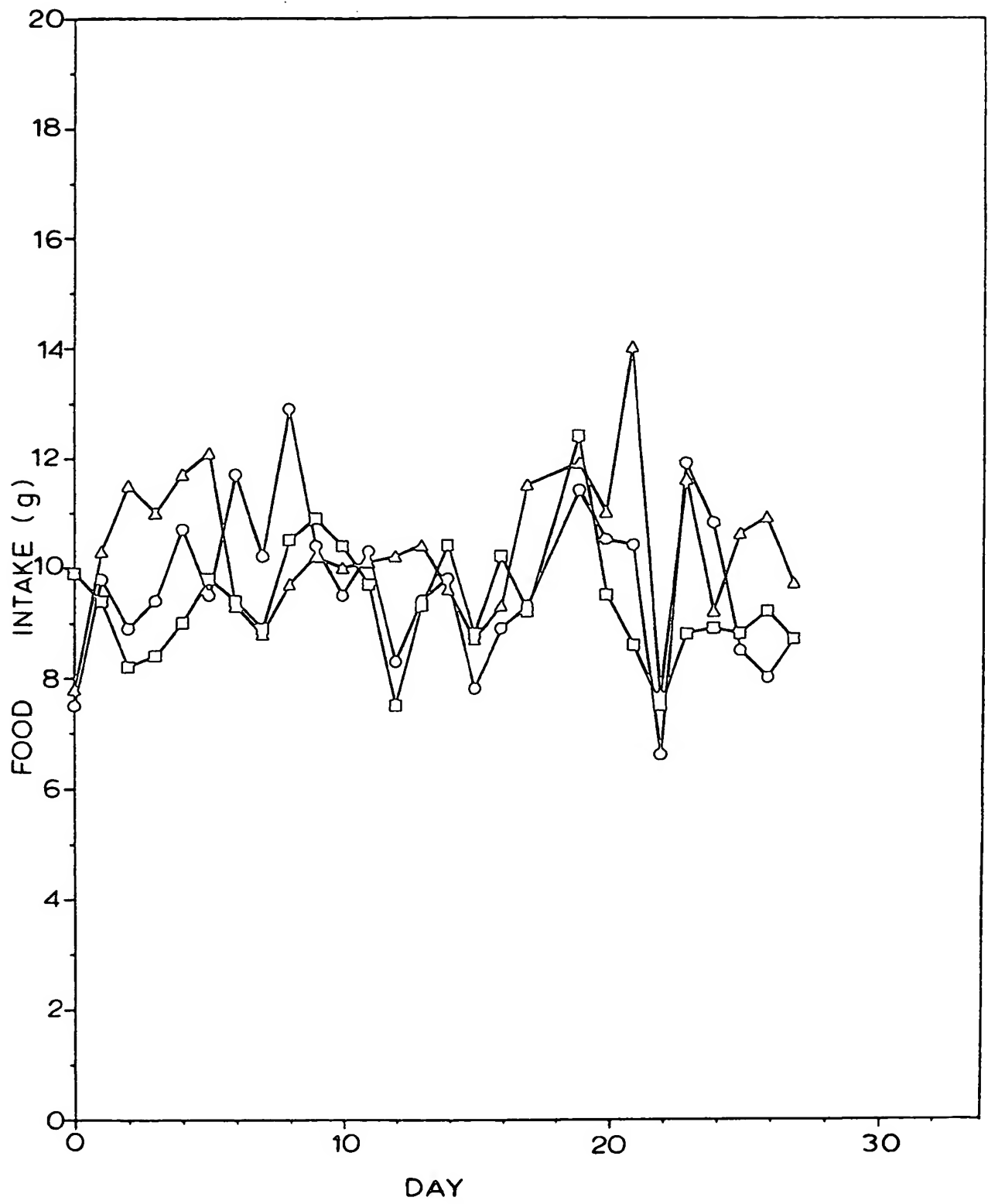


FIG.28C

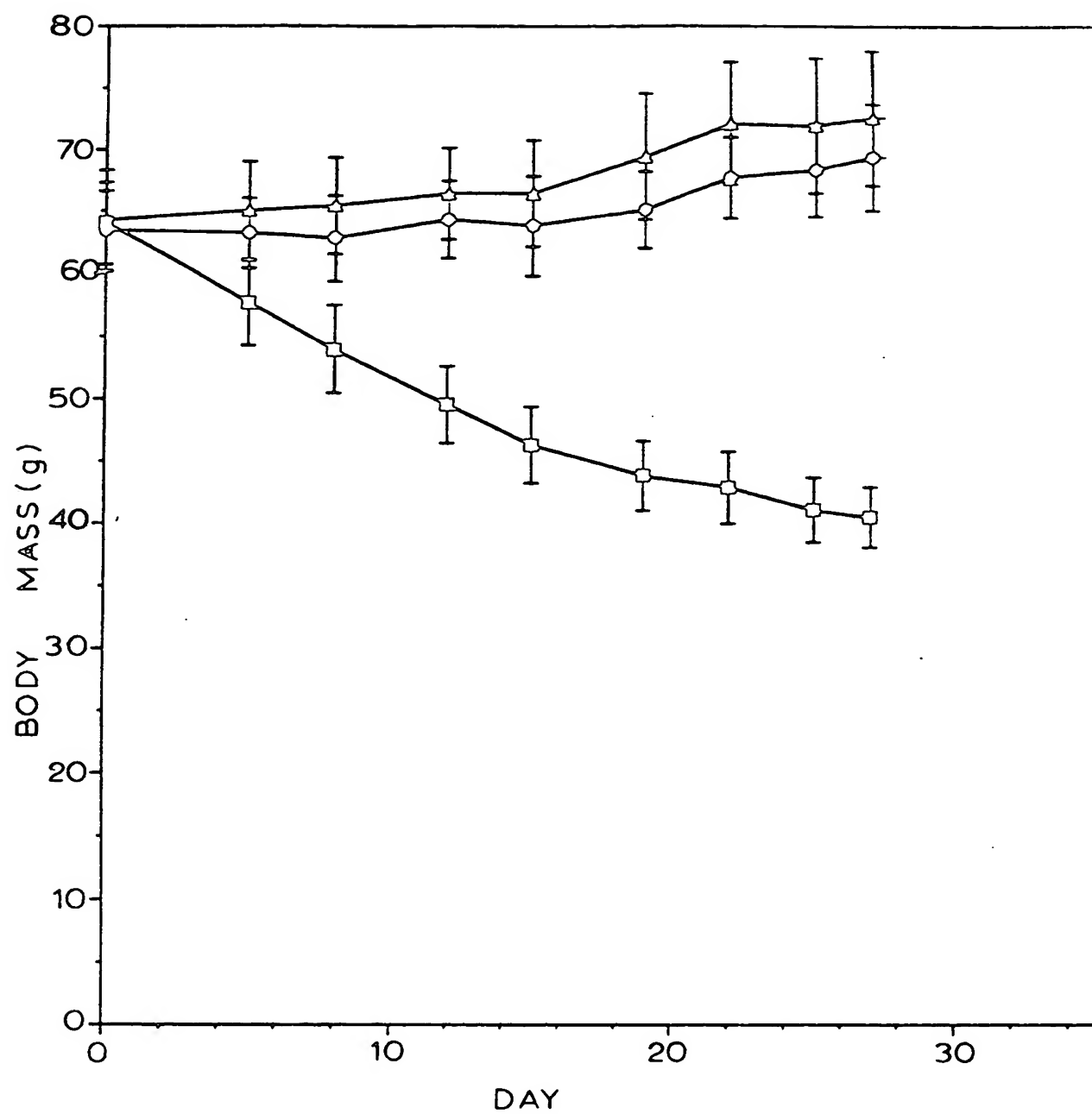


FIG.28D

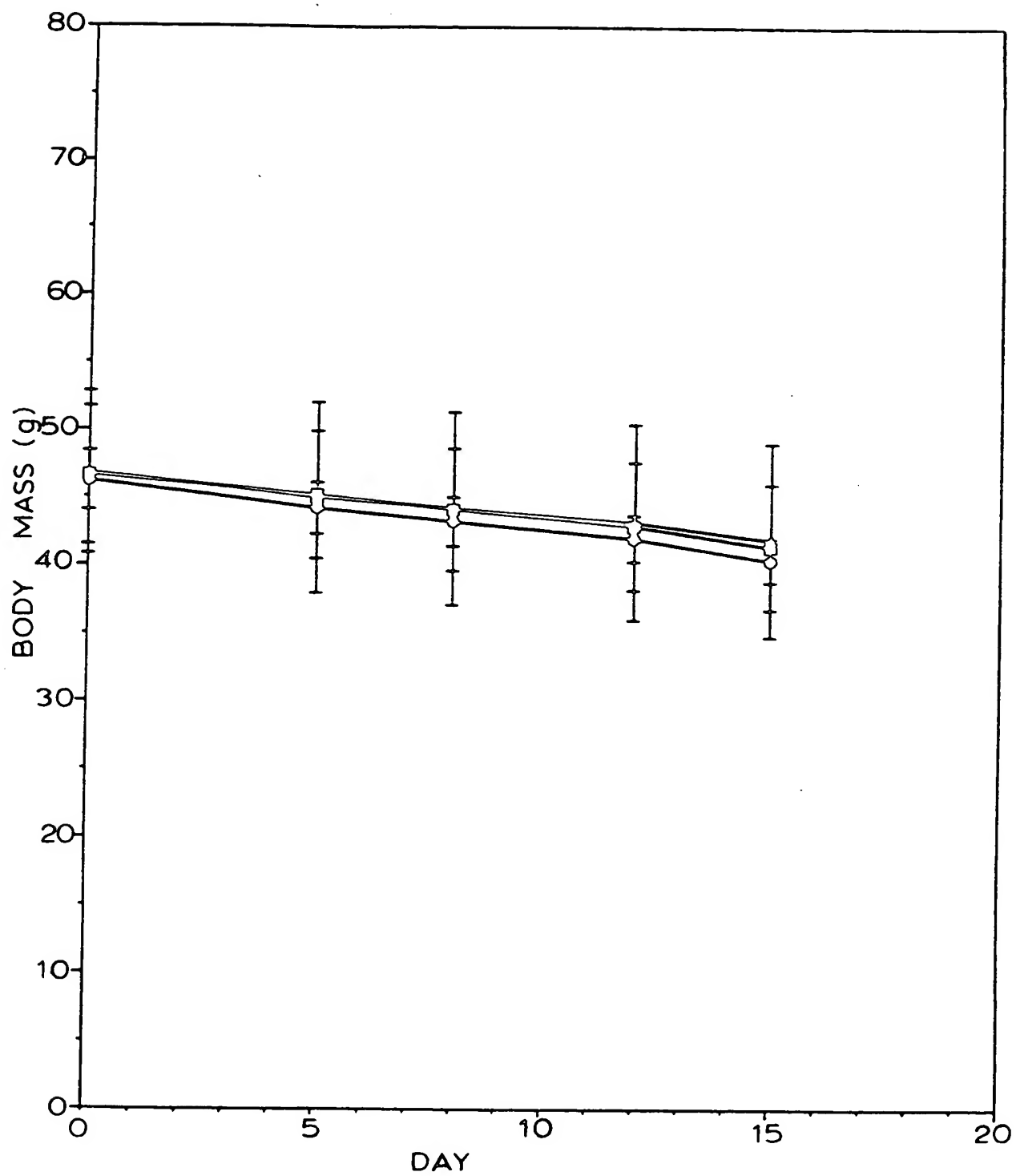


FIG.28E

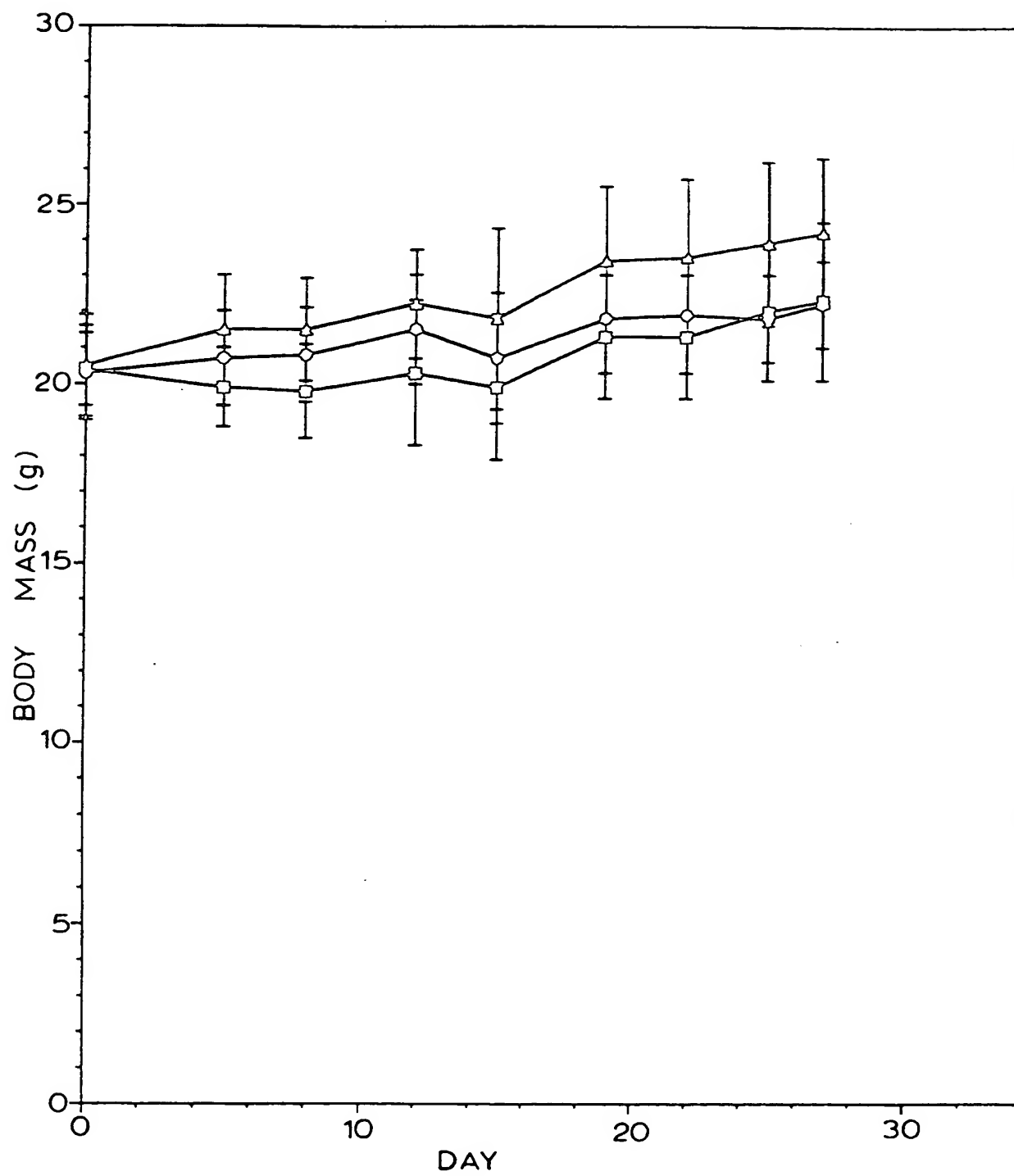


FIG.28F

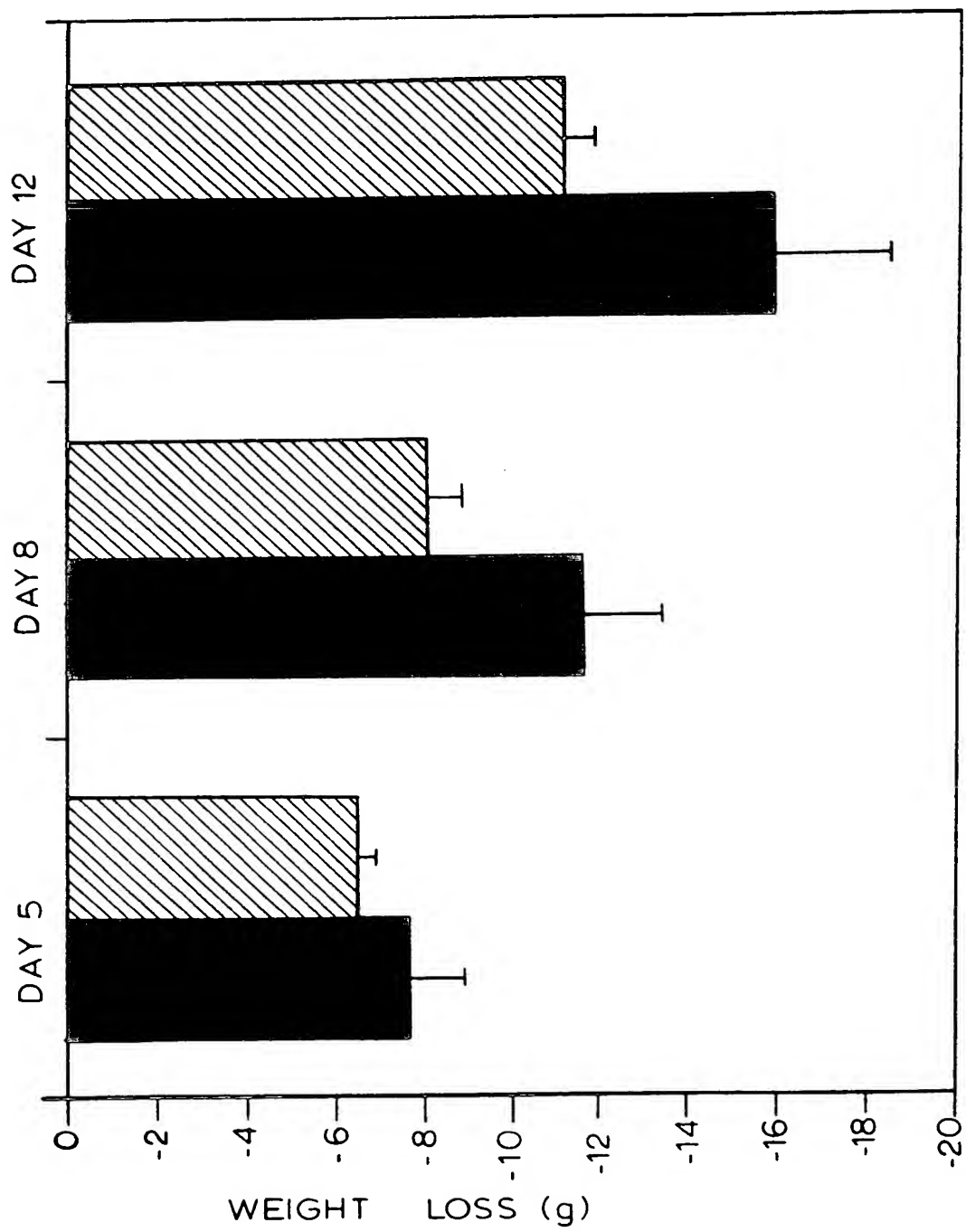


FIG. 29A

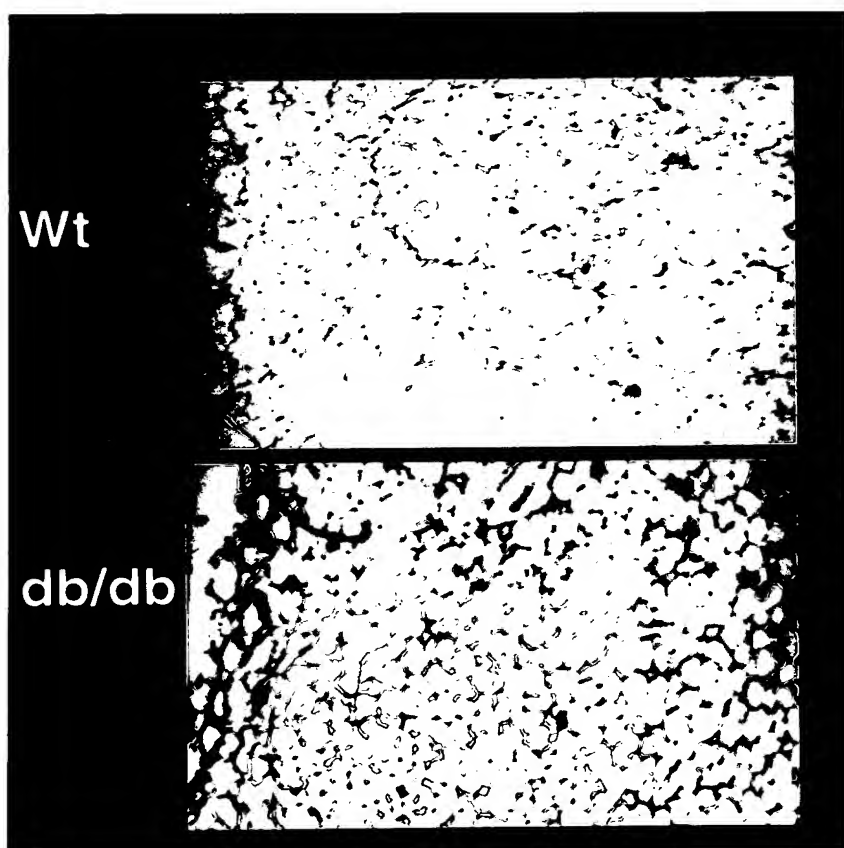


FIG.30



FIG.29C



FIG. 29B

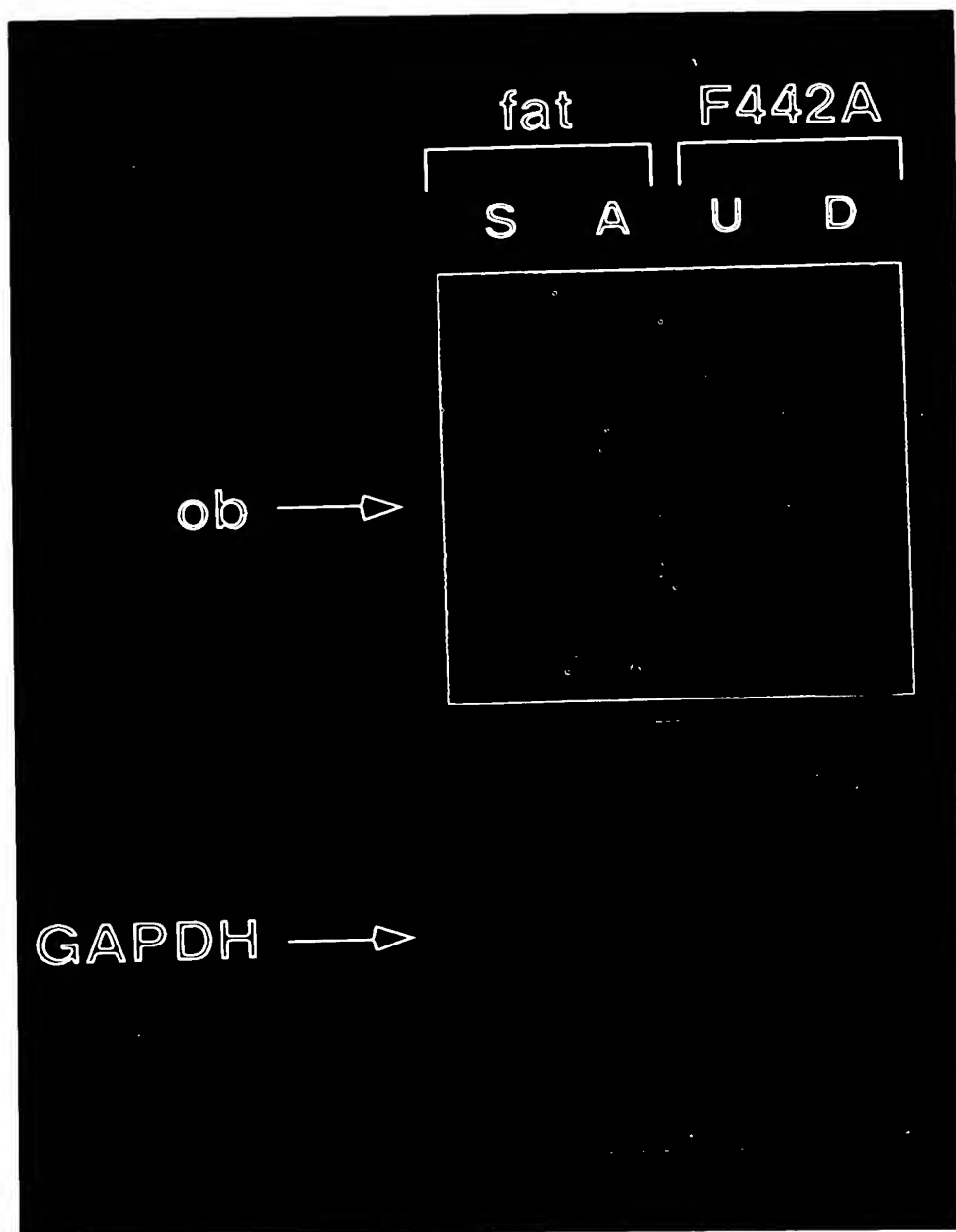


FIG.31.

1 2 3 4

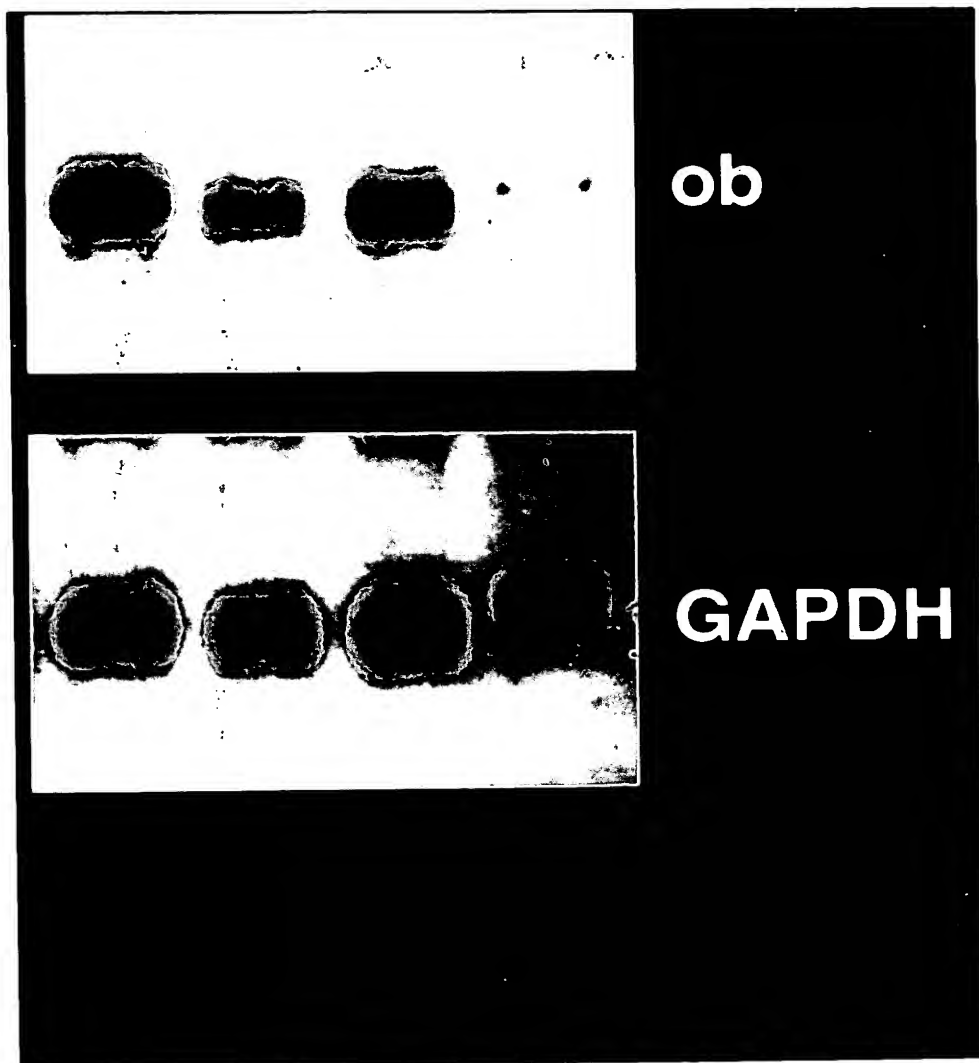


FIG.32A

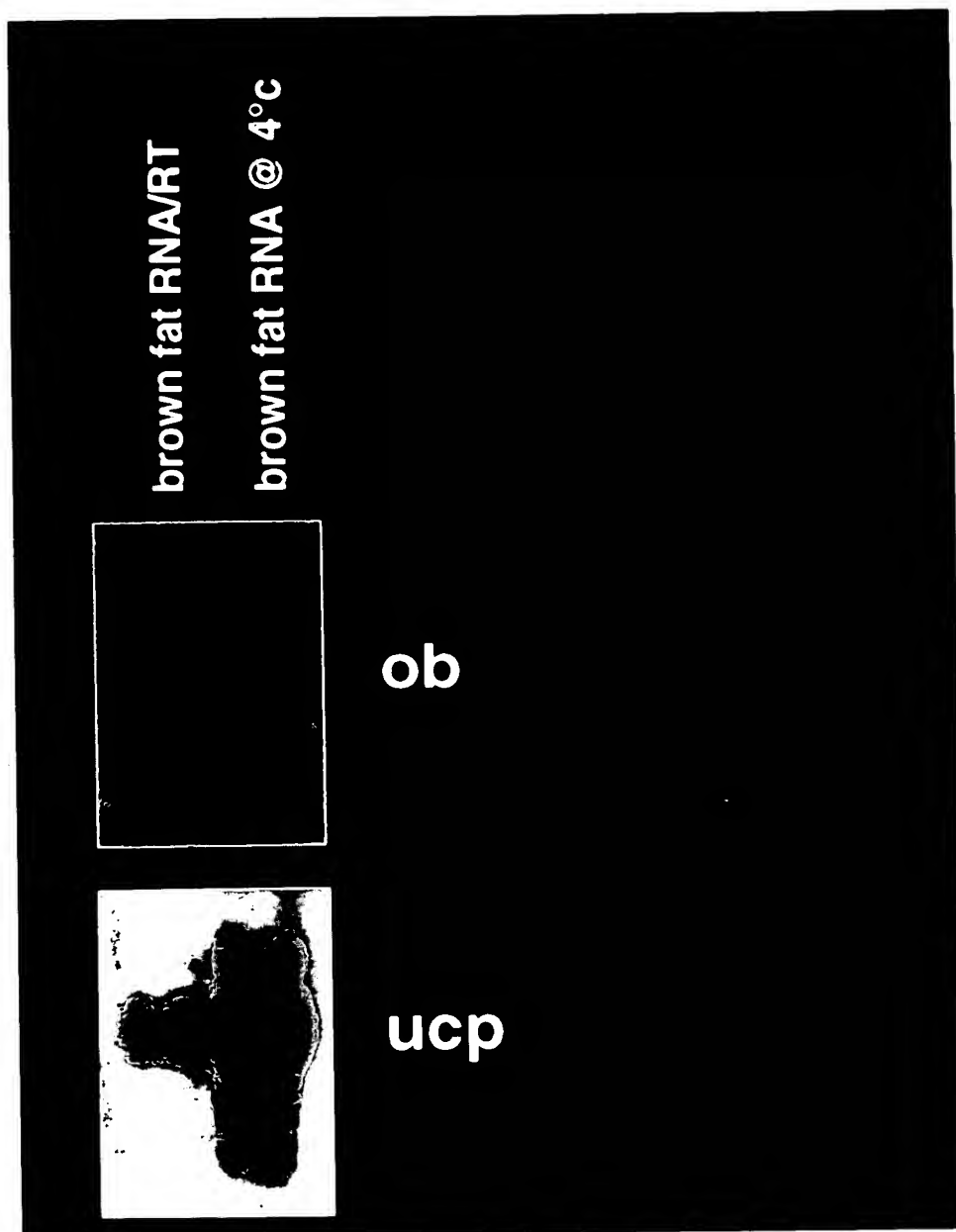


FIG.32B

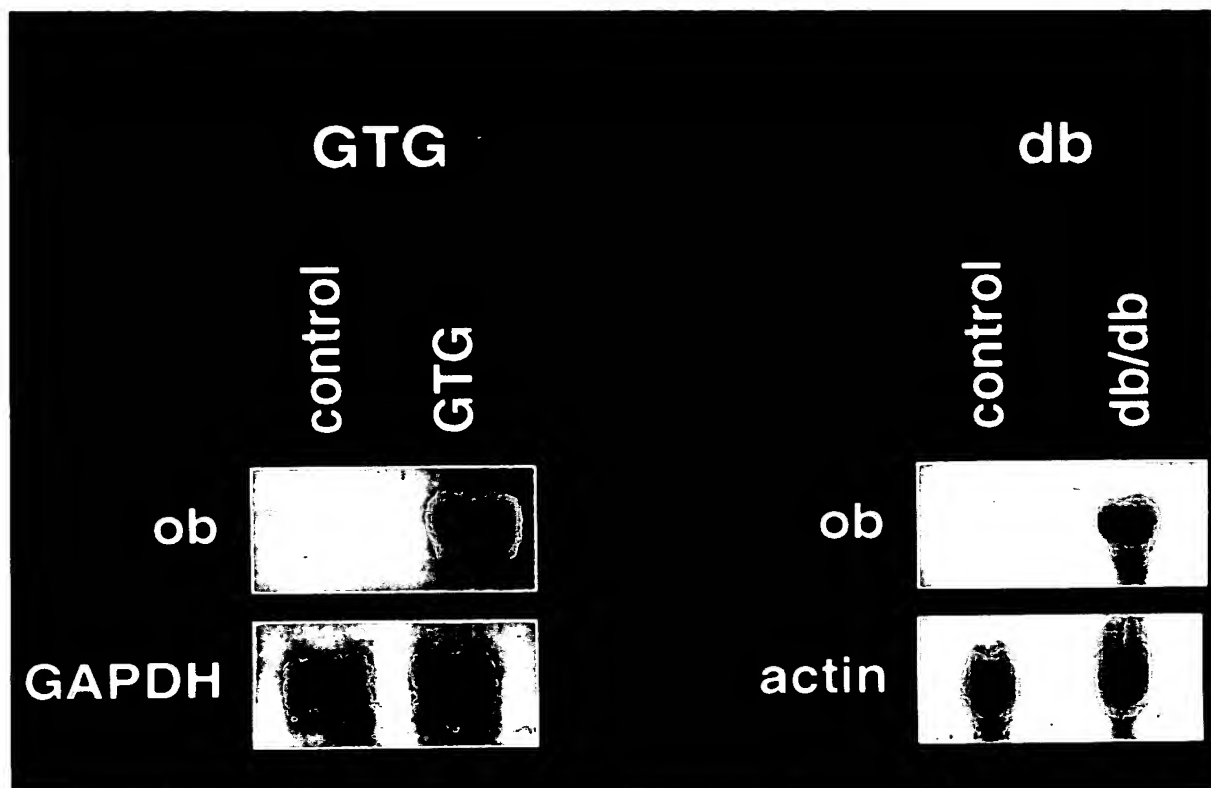


FIG.33

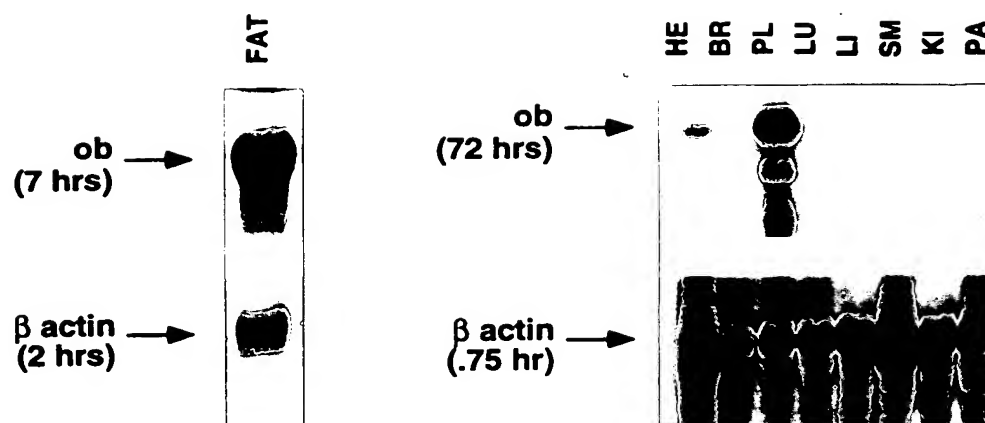


FIG.34

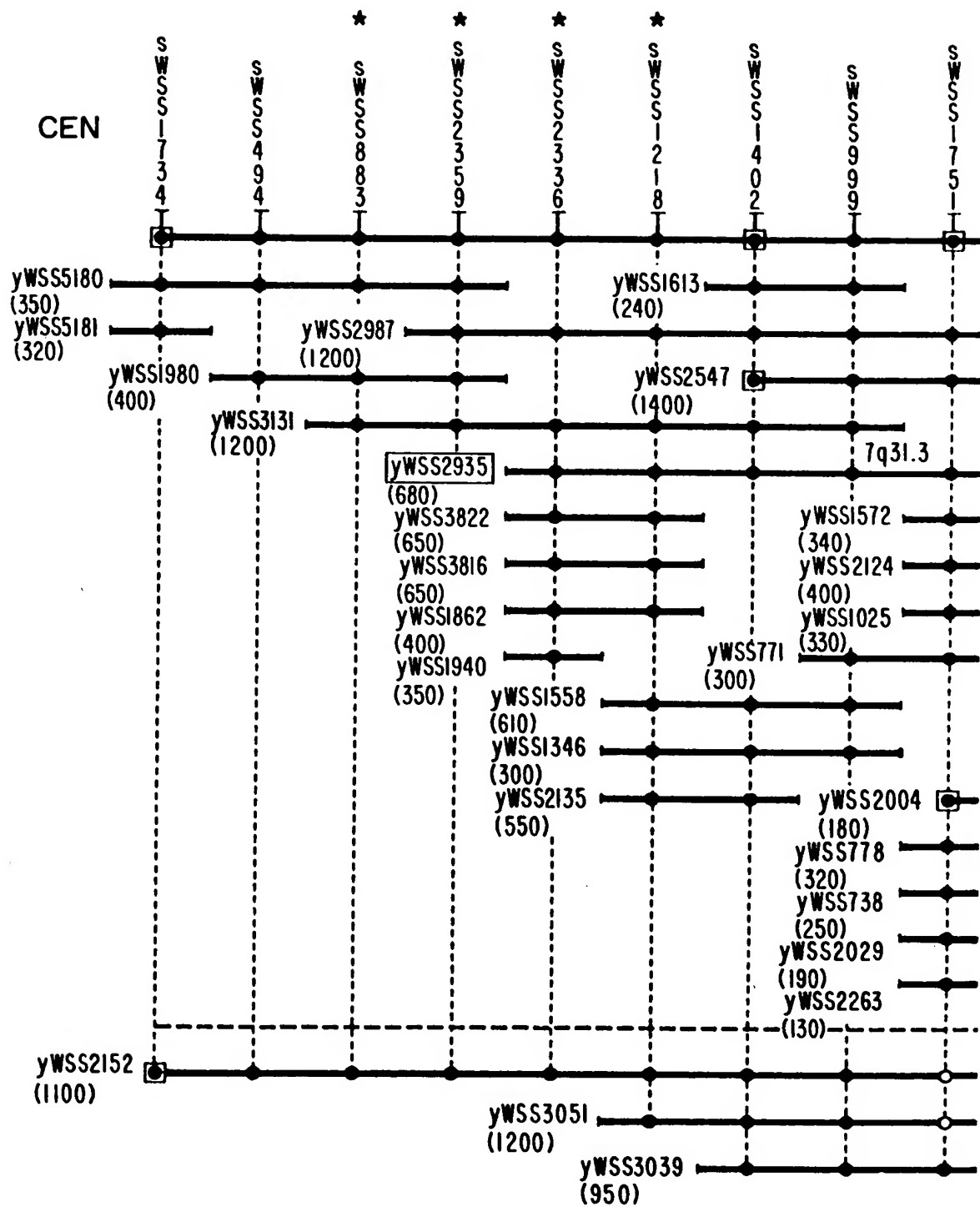


FIG. 35A

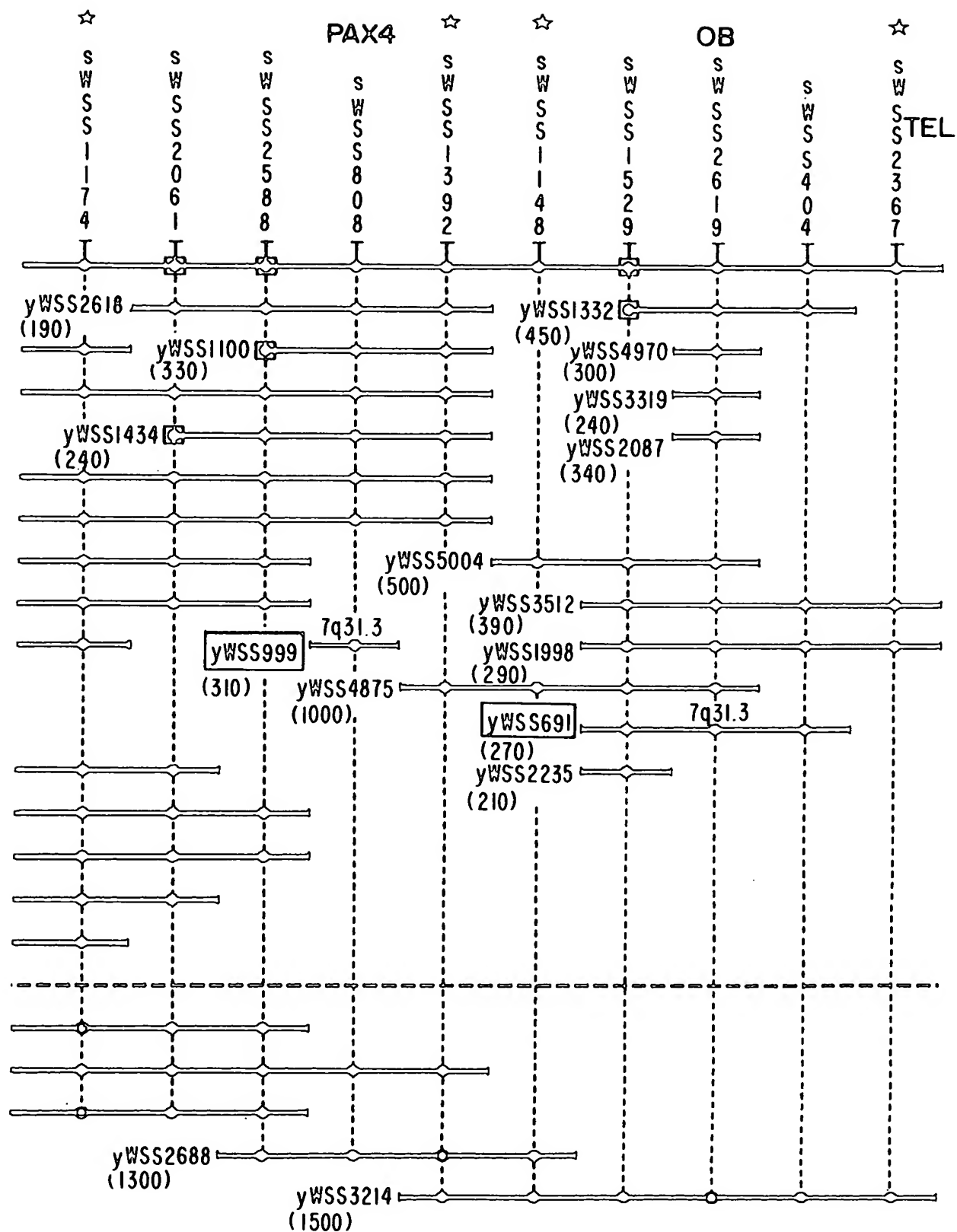


FIG. 35B